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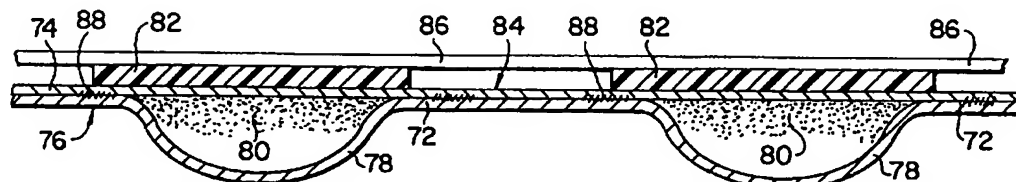
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(54) Title: CONTAINERS FOR INDIVIDUAL DOSES OF AN INHALABLE PHARMACEUTICAL



(57) Abstract: A dose strip (60) for use with a powder inhaler (50) includes a base strip (76) having spaced apart blisters (78) containing a pharmaceutical powder (80). A lid strip (84) is attached over the base strip (76), sealing the pharmaceutical powder (80) within the blisters (78). Lid tabs (82) are attached to the lid strip (84) over each blister. A peel strip or string (86) is joined to each lid tab (82). The dose strip (60) is preferably wound into a compact coil, so that it may be contained within an inhaler (50). To access a dose of pharmaceutical powder (80), the peel strip (86) is pulled away from the base strip (76) and lid strip (84), causing a lid tab (82) to shear open the lid strip (84). The peel strip (86) and attached lid tabs (82) are wound on a first take up reel (62), and the base strip (76) and lid strip (84) are separately wound on a second take up reel (64), within the inhaler (50), after a dose within each blister is accessed.

DESCRIPTION

Containers For Individual Doses Of An Inhalable Pharmaceutical

Background Of The Invention

5 The field of the invention is powder storage devices and systems for storing and delivering pharmaceutical powders.

Inhalers have long been used to deliver pharmaceuticals via delivery into the lungs. Inhalation of a pharmaceutical may have several advantages over other delivery methods, such as delivery orally, or by injections. Pharmaceuticals taken orally may require larger doses, take longer to act within the body, or suffer from other disadvantages. Some
10 similar disadvantages are associated with injections, over and above the risks and disadvantages of using needles to provide injections.

Inhalation of pharmaceuticals has largely been provided using metered dose inhalers. Metered dose inhalers used compressed propellant gases to move a pharmaceutical from the inhaler into the patient's lungs. However, metered dose inhalers
15 have several disadvantages including difficulties among some patients in coordinating inhalation with release of the dose, variations in the dose delivered, and the use of propellant gases harmful to the environment.

As an alternative to metered dose inhalers, dry powder inhalers have also occasionally been used. Dry powder inhalers typically rely on the inhalation of the patient
20 to draw a dry powder pharmaceutical from the inhaler into the patient's lungs. Recently, significant advances in dry powder inhaler technology have been made, resulting in inhalers which more efficiently deliver pharmaceutical doses, and without some of the disadvantages of metered dose inhalers. See, for example, U.S. Patent Nos. 5,327,883, and 5,577,497. These and other dry powder inhalers use cassettes or disks having
25 individual doses of pharmaceutical powder which are separately delivered to the patient. While these types of delivery devices work well, they are limited in the number of doses which can be stored within a given space. As certain pharmaceuticals must be frequently used, it would be advantageous to provide pharmaceutical powder storage and delivery devices capable of providing an increased number of doses within a compact space.

30 Another factor with dry powder inhalers is the need to keep the pharmaceutical powder well sealed from the environment, to prevent contamination, caking, etc., until it is to be used by the patient. On the other hand, the individual dose container used in a dry powder inhaler must be reliably and easily opened when it is time for the individual dose to be used. In addition, during opening of the individual dose container, the container
35 packaging must avoid contaminating the pharmaceutical powder, i.e., via particles, fibers, etc., from the packaging mixing with the inhaled pharmaceutical powder.

A primary source of instability of drug formulations packaged in blister packages is moisture or water vapor ingress into the blister package. As water vapor penetrates into the blister package, it may induce physical instability, resulting in adverse effects (such as caking, clumping, particle growth, etc.) on the performance of the drug formulation. Consequently, when the blister package is used in an inhaler, a full dose may not be delivered to the patient.

Foil-based blister packages, due to their sealed nature, are often expected to provide a complete physical barrier to moisture or water vapor ingress. Although materials are available that have very low moisture transmission rates, water vapor can still penetrate blister packages made with even the most impermeable of materials. This occurs primarily through the edges of the package or laminate structure. Over time, water vapor enters the blister by migrating through the adhesive joining the layers of materials. Despite the advances in polymer materials reducing the affects of migration of water over time through the laminate structure remains as a significant challenge. Indeed, most blister packages now generally require a secondary overwrapping, bag, or sealed foil package, to protect the blister package from moisture ingress, during shipment and storage.

Accordingly, it is an object of the invention to provide improved pharmaceutical powder storage and delivery devices, for use with a dry powder inhaler.

Brief Statement Of The Invention

To these ends, in first aspect of the invention, a dose strip for use with a powder inhaler includes a base strip having spaced apart blisters holding a pharmaceutical powder. A lid strip is attached to the base strip and seals the powder within the blisters. A lid tab is attached to the lid strip over each of the blisters. A peel strip is joined to each peel tab. The dose strip is preferably coiled up in a round or serpentine configuration so that a large number of doses can be provided within a small space.

In a second aspect of the invention, the dose strip may use small drums containing a pharmaceutical powder, instead of blisters.

In a third and separate aspect of the invention, blisters are formed in a head plate. Movement of a plunger unseals and releases powder contained in the blisters.

In a fourth aspect of the invention, dose strips have powder contained or entirely sealed within blisters or cups. Each individual dose is accessed and released via mechanical actuation.

In a fifth aspect of the invention, a container for pharmaceuticals includes a carrier, and a foil laminate. The foil laminate contains a first and second layer of metal foil, with

one of the first and second layers adhered to the carrier and the foil laminate terminating in an outer edge. One or more blisters are located between the first and second layers of metal foil for the storage of the pharmaceutical. The path length of each of the one or more blisters to the outer edge of the foil laminate is preferably at least 1.0 cm. In addition, a portion of the region of the foil laminate between the one or more blisters and the outer edge of the foil laminate is tortuously shaped.

In a sixth aspect, the foil laminate is formed to provide an increased path length between the edges of the foil laminate and the blisters, while retaining a compact size and shape.

In a seventh aspect of the invention, a method of making a carrier for pharmaceuticals includes the steps of providing a carrier and a foil laminate having one or more blisters containing the pharmaceutical formulation. The foil laminate contains a first and second layer of metal foil and has an outer edge, wherein the path length of each of the one or more blisters to the outer edge of the foil laminate is preferably at least about 1.0 cm. One of the a first and second layers of the foil laminate is fixed to the carrier. The method also includes the step of forming a tortuous pathway between the one or more blisters and the outer edge of the foil laminate.

In an eighth aspect of the invention, the method similar to the fourth aspect includes the step of providing a foil laminate having an inner edge and an outer edge, and forming a tortuous pathway between the one or more blisters and the inner edge of the foil laminate.

The invention resides as well in subcombinations of the elements described.

Brief Description Of The Drawings

- Figure 1 is a perspective view of a dry powder inhaler;
Figure 2 is a schematic plan view of a dose strip within an inhaler;
Figure 3 is a plan view of the dose strip shown in Figure 2;
Figure 4 is a section view thereof;
Figure 5 is a bottom view thereof;
Figure 6 is a perspective view of a drum for containing a dose of pharmaceutical powder;
Figure 7 is a side view thereof;
Figure 8 is a perspective view of a dose strip having drums as shown in Figure 6;
Figure 8A is a front view of the dose strip of Figure 8;
Figure 9 is a schematic perspective view of a cartridge having the drums shown in Figure 6 used with an inhaler;

Figure 10 is a perspective view of an alternative drum embodiment before delivery;

Figure 11 is a perspective view thereof during delivery of the drug dose;

Figure 12 is a perspective view of another drum embodiment before delivery;

5 Figure 13 is a perspective view thereof showing the drum during delivery of the dose of pharmaceutical powder;

Figure 14 is a partial perspective view of an alternative dose strip embodiment, before delivery of a dose of pharmaceutical powder;

Figure 15 is a partial perspective thereof during delivery;

10 Figure 16 is a perspective view of an alternative dose strip design;

Figure 17 is an enlarged front view thereof;

Figure 18 is a perspective view of an inhaler having the dose strip shown in Figure 16;

Figure 19 is an exploded perspective view of another dose strip embodiment;

15 Figure 20 is a perspective view showing operation of the dose strip of Figure 19;

Figure 21 is a perspective of an inhaler using the dose strip shown in Figure 19;

Figure 22 is a side view of an alternative embodiment dose strip;

Figure 23 is a perspective view of the slider shown in Figure 22;

20 Figure 24 is a perspective view of an inhaler using the dose strip shown in Figure 22;

Figure 25 is a perspective view of another dose strip embodiment;

Figure 26 is a partial section view thereof;

Figure 27 is perspective view showing an inhaler using the dose strip shown in Figure 25;

25 Fig. 28 is a perspective view of section of an alternative dose strip embodiment;

Fig. 29 is a top view thereof;

Fig. 30 is a side view thereof;

Fig. 31 is a front or end view thereof;

Fig. 32 is a schematic illustration of an alternative inhaler;

30 Fig. 33 is a geometric construction illustrating operational features of the inhaler shown in Fig. 32;

Fig. 34 is an enlarged side view of the track shown in Fig. 32;

Fig. 35 is a perspective view of a section of another dose strip embodiment;

Fig. 36 is a side view thereof;

35 Fig. 37 is a top view thereof;

Fig. 38 is an end view thereof;

Fig. 39 is a perspective view of segment of another dose strip embodiment;

- Fig. 40 is a top view thereof;
Fig. 41 is a side view thereof;
Fig. 42 is an end view thereof;
Fig. 43 is a perspective view of another inhaler embodiment;
5 Fig. 44 is an enlarged top view thereof;
Fig. 45 is a top view of a dose strip for use in the inhaler shown in Fig. 43;
Fig. 46 is a side view thereof;
Fig. 47 is a section view taken along line 47-47 of Fig. 44;
Fig. 48 is an exploded perspective view of a segment of another dose strip
10 embodiment;
Fig. 49 is a side view thereof, with several of the blisters or containers shown;
Fig. 50 is a top view thereof;
Fig. 51 is an end view thereof;
Fig. 52 is a perspective view of an inhaler having a blister inverter device;
15 Fig. 53 is a schematic view of a blister shown in Fig. 52, before opening;
Fig. 54 is a schematic view of the blister shown in Fig. 52, after opening;
Fig. 55 is a plan view of an alternative blister for use in the inhaler shown in Fig.
52;
Fig. 56 is a partial bottom view of a blister disk for use in the inhaler shown in Fig.
20 1;
Fig. 57 is an exploded perspective view of the blister disk shown in Fig. 56;
Fig. 58 is a section view of a blister container;
Fig. 59 is a diagram of the path length of the blister disk shown in Fig. 58;
Fig. 60 is a perspective view of another blister container;
25 Fig. 61 is a diagram illustrating the path length for the outer and inner edges of the
blister package of Fig. 60;
Fig. 62 is a perspective view of another blister package;
Fig. 63 is a diagram illustrating the path length for an edge of the blister package of
Fig. 62;
30 Fig. 64 is a perspective view of another blister package;
Fig. 65 is a diagram illustrating the path length for the outer and inner edges of the
blister package of Fig. 64;
Fig. 66 is a perspective view of another blister package;
Fig. 67 is a diagram illustrating the path length for the outer and inner edges of the
35 blister package of Fig. 66;
Fig. 68 is a perspective view of another blister package;

Fig. 69 is a diagram illustrating the path length for the outer and inner edges of the blister package of Fig. 68;

Fig. 70 is a partial plan view of another blister package;

Fig. 71 is a diagram illustrating the path length for the outer and inner edges of the blister package of Fig. 70;

Fig. 72 is a partial plan view of another blister package;

Fig. 73 is a diagram illustrating the path length for the outer and inner edges of the blister package of Fig. 72; and

Fig. 74 is a partial plan view of another blister package.

10 Detailed Description Of The Drawings

Turning now in detail to the drawings, as shown in Figure 1, an inhaler 50 has a housing 52 and a mouthpiece 54. An advancing knob 56 on top of the housing 52 is used for advancing individual doses of a powder pharmaceutical, for inhalation by a patient. Various equivalent advancing mechanisms using cams, gears, indexing springs or fingers, sliding or pivoting components, may also be used.

Referring to Figures 1-5, a dose strip or tape 60 is supported within the housing 52 on a spool 58. The dose strip 60 includes a base strip 72 having spaced apart blisters 78 containing a pharmaceutical powder 80. A lid strip 74 is attached to the base strip 72. The base strip 72 and lid strip 74 are sealed together in a circumferential seal area 76 surrounding each of the blisters 78, to seal the pharmaceutical powder 80 from the environment. The base strip 72 and lid strip 74 are preferably a thin metal foil, such as aluminum or foil/plastic laminate. A lid tab 82 is attached to the lid strip 74 over each of the blisters 78. The lid tab 82 is preferably metal or hard plastic. A peel string 86 is attached to each of the lid tabs 82 along the length of the dose strip 60. The peel string 86 may be adhered to or imbedded within the lid tabs 82, or it may be intermittently tacked with an adhesive. Alternatively, the string 86 can be "attached" by threading it through the lid tabs 82. The lid tabs 82 are spaced apart by a joining segment 84 made of the base strip 72 and lid strip 74, so that the dose strip 60 can be rolled or coiled up into a compact configuration. A peel perforation 88 is optionally provided at the leading forward edge of each of the lid tabs 82. The peel perforation 88 may take the form of a perforation or an indentation in the lid strip 74 at the front edge of each lid tab 82. Attachment tabs may be used in place of the string 86.

Referring back to Figure 2, in use, the peel string 86 is wound around a peel string take up reel 62, while the rest of the dose strip 60 is wound around a base strip take up reel 64. The dose strip 60 preferably has a lead in section without blisters 78, or lid tabs 82, to

better facilitate winding the peel string 86 onto the peel string take up reel 62 and winding the base strip 72 and lid strip 74 onto the lid strip take up reel 64.

To advance the dose strip 60 to deliver a dose of pharmaceutical powder 80, the advancing knob 56 or other mechanism is turned or otherwise moved, thereby causing the
5 spool 58 to index one position clockwise (in Figure 2) while the peel string reel 62 indexes one position counter clockwise. As this occurs, the peel string 86 pulls the next lid tab 82 away from the base strip 72 and lid strip 74, causing the lid strip 74 over the blister 78 to shear away from the remaining lid strip 74 surrounding the blister. As the blister is opened at a delivery station 90 within the housing 52, the pharmaceutical powder 80 falls
10 into a mixing chamber, or into a duct leading to a mixing chamber, for mixing with air inhaled by the patient. Alternatively, the powder can be entrained in an air flow and removed from the blister.

The peel perforation 88 provides a location on the lid strip 74 having reduced shear strength, thereby reducing the force required to shear open the blisters 78. As the dose
15 strip 60 is advanced to deliver the pharmaceutical powder within each subsequent blister 78, the peel string 86 and lid tabs 82 attached to the peel string 86 are wound and stored on the peel string reel 62. The base strip 78 and lid strip 74 (less the sheared out blister lids which remain adhered to the underside of the lid tabs 82) are wound around and stored on the lid strip take up reel 64. A crushing wheel 66 flattens out the spent blisters 78 before
20 they are wound onto the lid strip take up reel 64, so that less space is required within the housing 52. The spent blisters could also be otherwise crushed (sliding, etc.) or nested to conserve room.

Referring now to Figure 8, in another dose strip embodiment 102, a carrier ribbon 104 has a back or base 106, and loop tabs 108. Each loop tab 108 holds a drum 114.

25 Referring momentarily to Figures 6 and 7, each drum 114 has a front flange 120 and a back flange 122 attached to a cylindrical body 116. A bore 118 within the cylindrical body 116 contains a pharmaceutical powder 80.

Referring to Figures 7, 8, and 8A, the pharmaceutical powder is sealed within the drum 114 via the folded over loop tabs 108. The inside surface 110 of the loop tab 108 is
30 attached on each side to the front and back flanges 120 and 122. This attachment may be via an adhesive, a heat-formed seal, or other peelable attachment. Each loop tab 108 has loop sides 124 joined to the base 106 and to a front web 126. The drum 114 is preferably attached to the web 126 with web flaps 128 secured around the cylindrical body 116 of the drum 114. This design could be made without web flaps 128. The drums could fall for
35 collection, or remain partially attached to loop tabs 128.

The dose strip 102 is preferably provided in a loop or coil which can be contained within an inhaler. Each drum 114 is ordinarily in a stored position, indicated by A in

Figures 8 and 8A. In the stored position, the inside surfaces 110 of the loop tabs 108 are sealed against the flanges 120 and 122, thereby sealing the pharmaceutical powder within the bore 118 against the environment. For delivery of the pharmaceutical powder within an inhaler, an actuator within the inhaler draws or pushes the drum 114 away from the base 106. As this occurs, the loop sides 124 unfurl and peel away from the flanges 120 and 122. With the drum 114 in the fully extended or open position, indicated by B in Figure 8, the bore 118 of the drum 114 is aligned with a flow path in the inhaler. Air flows through the bore 118 carrying out the pharmaceutical powder for inhalation. Thereafter, the actuator moves the now empty drum 114 back into the stored position A, for compact storage of the dose strip 102 within the inhaler. After all of the drums 114 are used and empty, the dose tape 102 is replaced.

Figure 9 shows an embodiment 138 similar to the dose strip 102 shown in Figure 8, except that the carrier ribbon 104 is formed into a disk 140. A central hub 142 of the disk 140 facilitates mounting the disk 140 within an inhaler. The actuator 146 in Figure 9 is shown as a radially acting actuator, for moving the drums from a stored position to a delivery or extended position, and then back to the stored position.

Referring to Figures 10 and 11, in an alternate drum design 148, a carrier 156 is sealed within the bore 118 by front and back end seals 150. The carrier 156 has a through hole 158 containing a dose of powdered pharmaceutical.

In use, the drum 148 is provided on a dose strip or disk and loaded into an inhaler. The inhaler has one or more plungers 152, optionally including a circular seal or an O-ring 154 adapted to closely fit within the bore 118. To deliver the dose of powdered pharmaceutical contained in the through hole 158, the plunger is driven through top or front end seal 150, as shown in Figure 11, thereby driving the carrier 156 through the bottom or back end seal 150 and out of the bore 118. The through hole 158 holding the powdered pharmaceutical dose is then advantageously aligned with an inhalation flow path. Air moving through the flow path passes through the through hole 158 and carries the pharmaceutical powder through the inhaler to the patient. The lower end of the carrier 156 preferably has a pointed end 160, to reduce the force required to eject the carrier 156.

The end seals 150 are securely attached to the flanges 120 and 122 of the drum 138 to seal the carrier containing the powdered pharmaceutical from the environment. However, the end seals 150 are sufficiently thin to allow the plunger 152 to pierce through them with nominal force. The end seals 150 are preferably a metal, such as aluminum, foil, although plastics and other materials can also be considered. The plunger 152 may also have a pointed end to facilitate piercing the front end seal 150.

Figures 12 and 13 show another alternative drum embodiment 162 having only a lower flange 166, and a carrier sealed within a blind bore 168 by a single end seal 150.

The drum 162 has a collapsible body 164 formed as a cylinder or other shape, such as e.g., a square or hexagon. This shape could contain convolutions to facilitate collapse. In use, a plunger 152 or other actuator within an inhaler pushes on the blind end of the drum 162, collapsing the body 164, as shown in Figure 13, and driving the carrier 156 through the end seal 150, to release a dose of powdered pharmaceutical from the through hole 158 into an air stream within the inhaler.

Figure 14 and 15 show another drum embodiment 170 having elongated drums or tubes 172 attached to a dose tape 176 by straps 178. A dose of pharmaceutical powder 80 is sealed within the tube 172 at one end by a plunger/seal plug 174 and by an end seal 180 at the other end. In use within an inhaler, the plunger 174 is pushed into the body of the tube 172, causing the end seal 180 to burst and allowing the pharmaceutical powder 80 to be ejected into a duct, mixing chamber, or other space in an inhaler. The tube 172 may be sealed on both sides with end seals 180, to better protect the powder 80 from the environment.

As shown in Figures 16, 17 and 18, another inhaler embodiment 208 uses a dose strip 182 having a head plate 184 which fits over a head plate housing 202. Blisters 186 are formed in the head plate 184. A pharmaceutical powder is sealed within each blister 186 via a blister seal 188 on the underside of the head plate 184. A plunger 190 is joined to each seal 188. Each plunger 190 has a longitudinal slot 192 which receives a finger 196 of a button 194, as shown in Figure 17. The head plate 184 and housing 202 form an inhalation flow path 204. The lower ends of the plungers 192 extend through clearance holes 206 in the housing 202. The dose strip 182 is installed in the inhaler 208, with a button 194 associated with each blister 186 extending outside of the inhaler case 209.

The inhaler 208 has an impeller 216 spinable within a disk-shaped mixing chamber 212. A motor 214 spins the impeller, as described, for example, in U.S. Patent No. 5,577,497. The front end of the inhaler 208 forms a mouthpiece 210.

In use, the patient pushes down on a button 194. The finger 196 correspondingly drives the plunger 190 down, shearing the seal 188 out of the underside of the blister 186. This releases the pharmaceutical powder 80 into the flow path 204. At the same time, the underside 198 of the button 194 moves down and crushes the blister 186, to assist in release of the pharmaceutical powder 80. The plunger moves down into alignment with the floor 205 of the housing 202, to avoid significantly obstructing the flow path. The patient then inhales through the mouthpiece 210, drawing in the dose of pharmaceutical powder 80, which travels through the flow path 204, into the mixing chamber 212 (where the powder 80 is mixed with air and/or de-agglomerated), and then is inhaled by the patient.

Another inhaler embodiment 218, as shown in Figures 19-21, includes a dose strip 220, somewhat similar to the dose strip 182, but having blisters 224 formed on a footplate 222. A plunger 226 is attached to a blister seal 225 at the top surface of the footplate 222. Each plunger 226 has a slotted head 228 adapted to fit into a slider 232, as shown in
5 Figure 20. The footplate 222 is secured within a tray 230. A slider plate 234 is attached to the tray 230, with the plunger heads 228 extending above the slider plate 234. An air path 236 is formed within the tray 230 and slider plate 234.

The tray 230 is placed within or attached to the inhaler 218. To operate the inhaler, the patient pushes the slider 232 rearwardly. As this occurs, the slider lifts the
10 first plunger 226 on the footplate 222. The plunger 226 shears or breaks open the seal 225 of the blister 224, exposing the dose of pharmaceutical powder. The patient inhales, drawing the dose through the air path 236, the mixing chamber 212 and the mouthpiece 210.

Referring to Figures 22-24, another inhaler 248 is somewhat similar to the inhaler
15 shown in Figure 18, except that a slider 260 is used to open the blisters 186. The flow path 204 is formed between the underside of the head plate 184 and a slide plate 258. A slider 260 has a wedge 262 which engages the slots 192 on the plungers 190. To release a dose of powdered pharmaceutical from a blister 186, the patient slides the slider 260 towards the back of the inhaler 248. The wedge 262 on the slider 260 pulls the plunger
20 190 down breaking the seal 225 and releasing the pharmaceutical powder into the flow path 204, for inhalation as described above.

Figures 25-27 show another inhaler embodiment 270 having a dose strip 274 including a block 276 with bores 278. Pegs 282 are placed within the bores 278. Each peg 282 has a dose reservoir 284 and a through hole 286. An upper seal 288 and a lower
25 seal 290 seal the reservoir 284 from the environment. The through hole 286 is aligned with a flow path 280 extending through the block 276.

In use, the dose strip 274 is placed into the inhaler 270, with the flow path 280 in the block 276 mating with an opening into the mixing chamber 212. To inhale a dose, the patient pushes the first peg 282 down, bringing the reservoir 284 into alignment with the
30 flow path 280. The through holes 286 in the remaining pegs 282 are aligned with the flow path 280, to avoid obstructing the flow path. The patient then inhales on the mouthpiece 210, drawing air through the flow path 280 and carrying the powdered pharmaceutical out of the reservoir 284 for inhalation as described above.

As shown in Figs. 28-31, in another dose strip embodiment 300, recesses or cups
35 304 are molded into a base strip 302. A lid 306 is attached to the base strip 302, via a hinge joint 308, at each of the spaced apart cups 304. The lid 306 includes a seal plate 310 dimensioned to press fit into the cup 304. A desiccant insert 314 may be provided on the

seal plate 310. A lift tab 312 extends upwardly at an angle from each lid 306, opposite the hinge joint 308. The dose strip 300 is preferably injection molded plastic.

Referring to Figs. 32-34, the dose strip 300 is used within an inhaler 320, similar to the inhaler shown in Fig. 1. The inhaler 320 includes a dose strip track 322 and an advancing mechanism 324. The dose strip track 322 has a base strip groove 326, and an opening groove 328. The vertical spacing between the base strip groove 326 and the opening groove 328 matches the nominal spacing between the base strip 302 and the lift tab 312 on the dose strip 300. However, at a peak section 330, the opening groove 328 moves farther away from the base strip groove 326, as shown in Fig. 34.

In use, the dose strip 300 is loaded into the inhaler 320, with the base strip 302 captured within the base strip groove 326, and with the lift tabs 312 within the opening groove 328. The advancing mechanism 324 advances the dose strip incrementally, e.g., by winding the base strip 302 about a drum. As the dose strip 300 moves through the track 322, the lift tab 312 is pulled out of its corresponding cup 304, as the lift tab 312 moves through the peak 330. The powder contained within the cup 304 then either falls, or is drawn out of the cup 304, and into a mixing or delivery chamber. If the dose strip 300 is positioned on its side, or right side up, the powder within the cup can be removed from the now opened cup 304 via air flow.

Turning to Figs. 35-38, a dose strip 350 is preferably manufactured out of one or two layers of foil, or foil/plastic laminates. The dose strip 350 has a base strip 352 linking dose cups 354 together. Base tabs 356 are provided on each side of the cylindrical body 358 of each dose cup 354. A lid 364 is attached to a body plate 360 at the top, or first end, of each cylindrical body 358 via a hinge 362. A seal plate 366 is dimensioned to provide a press fit with the cylindrical body 358. A lift tab 368 is provided on the lid 364 opposite the hinge 362. In use, the dose strip 350 is used in a way similar to the dose strip 300 shown in Fig. 28. The dose strip 350 is incrementally advanced within an inhaler, such as the inhaler 320. The base tabs 356 are captured within the base strip groove, while the lift tabs 368 move within the opening groove 328. As each dose container or cup 354 moves into the peak 330, the lid 364 is lifted off of the body plate 360, allowing pharmaceutical powder contained within the cup 354 to be removed, or flow out into another area of the inhaler, for inhalation.

Fig. 33 shows the movement of the lift tab 312 of the dose strip 300, or the movement of the lift tab 368 of the dose strip 350, as the lift tab moves the peak section 330 of the track 322. The lift tab 312 or 368 is lifted, or separated from the cup by an angle of about 10-45 degrees, and typically about 15-20 degrees, as shown in Fig. 33.

Turning to Figs. 39-42, a dose strip 380 includes a base strip 382 and a seal strip 386. The base strip 382 has equally spaced apart cups 384, as with the embodiment shown

in Figs. 28 and 35. The seal strip 386 has seal plates 388 which extend partially into the cups 384. After the cups 384 are filled with a pharmaceutical powder, the seal strip 386 is placed over the base strip 382, and the seal plates 388 are pressed partially into the cups 384. This press or interference fit between the seal plates 388 on the seal strip 386 and the cups 384 holds the seal strip 386 together with the base strip 382. Alternatively, an adhesive or heat seal 390 may optionally be used continuously or intermittently between the base strip 382 and seal strip 386. In use, with the dose strip 380 in an inhaler, as shown, for example, in Figs. 1 and 2, the seal strip 386 is peeled away from the base strip 382, to open each successive cup or container 384, in the same manner as the dose tape or strip 60 shown in Fig. 2.

Referring to Figs. 43-47, a dose strip 430 is used with an inhaler 400. The dose strip 430 includes blisters or cups 432 on a blister layer or strip 434. The blisters 432 contain a dry powder pharmaceutical. The blisters 432 are sealed with a seal layer or strip 436 adhered or heat sealed to the blister strip 434. The dose strips 300, 350 or 380 described above contain powder within a space via a press fit between a seal plate and the container or cup. Although the seal provided in those dose strips is sufficient to contain powder, the seal is not complete, and water vapor can penetrate into the containers. The fit between the plastic or metal foil materials is not sufficient to keep out water vapor. For some pharmaceuticals, penetration of water vapor into the powder is acceptable. However, for other pharmaceuticals, or for certain applications, it may be necessary to completely seal the pharmaceutical powder from the outside environment. The dose strip 430, unlike the dose strips 300, 350 and 380, provides such a substantially complete seal.

The inhaler 400 includes an advancing mechanism 402 having pins 405 on a drive wheel 403. The pins 405 engage drive holes 438 in the dose strip 430. A powder chamber 404 is provided in the inhaler 400 near a mouthpiece 407. A knife 406 is fixed in place within the inhaler 400 near the powder chamber 404.

A diamond shaped roller 408 is rotatably supported on an axle 414 in the inhaler 400. The roller 408 has first and second flat surfaces 410 and 412, intersecting each other at an angle B of from 90-150 degrees, and preferably 110-130 degrees. A first side roller 416 is rotatably supported on a first side axle 418, and has a roller surface 420 parallel to the first surface 410 of the roller 408. Similarly, a second side roller 422 is rotatably supported on a second roller axle 424, and has a second roller surface 426 parallel to the second surface 412 of the diamond shaped roller 408. The side roller surfaces 420 and 426 are spaced apart from the diamond shaped roller surfaces 410 and 412 by a gap equal to the thickness T of the side areas dose strip 430 (adjacent to the holes 438).

In use, the dose strip 430 is loaded onto a feed spool 440 and takeup spool 442 in the inhaler 400, as shown in Fig. 43. As the advancing mechanism 402 is actuated, the

drive wheel 403 advances the dose strip 430, via the pins 405 engaging the drive holes 438 in the dose strip 430. A blister 432 is pulled past the knife 406, which severs the blister along its centerline. As the severed blister advances, the sides of the dose strip are drawn in between the diamond shaped roller 408 and the side rollers 416 and 422. This causes
5 the dose strip segment around the blister 432 to be temporarily bent into a V-shape. As a result, the two halves of the severed blister are pulled apart from each other as shown in Fig. 47, allowing the pharmaceutical powder within the blister to fall into the powder chamber 404, for inhalation. When the dose strip 430 is next advanced, the now empty blister moves off of the diamond shaped roller 408. The segment of the dose strip around
10 the empty blister then reverts back to its flat configuration, with the now empty halves of the blister moving back together. As the dose strip 430 advances to deliver each successive dose, the severed and emptied blisters are wound onto the takeup spool 442. The strip could also be advanced by using the blisters themselves, indexed into conical holes on an advancing wheel.

15 Turning to Figs. 48-51, a dose strip 450 includes a second or blister strip or layer 454 adhered to a first or base strip or layer 452, and a third or seal strip or layer 456 adhered to the second layer 454. The base strip 452, which is preferably made of plastic, has equally spaced apart dimples or cones 460, which may be molded or pressed in. The dimples 460 are severed or cut through at a cut line 462, through the center of each
20 dimple. Perforations 464 preferably extend on the base strip 452 between the dimples 460, parallel to, and in alignment with, the cut lines 462. The second or cup strip 454 is placed over the base strip 452. Cups or blisters 466 (preferably cone-shaped) are preferably formed in the cup strip 454 by pressing the material of the cup strip overlying the dimples 460 into the dimples. The cup strip 454 is then preferably adhered or heat
25 sealed onto the base strip 452. The cups or blisters 466 are then filled with a pharmaceutical powder, and are sealed by adhering or heat sealing the seal strip 456 onto the cup strip 454. The powder within the dose strip 450 is substantially entirely sealed between the cup strip 454 and seal strip 456, which are both advantageously made of a metal foil or foil/plastic laminate. As shown in Fig. 50, wedge-shaped cutouts 470 are
30 made on the front side 476 of the center line 475 of the dose strip 450, forming discrete tabs 472, with one tab 472 associated with each cup 466, and dividing the strip into individual segments 476.

In use, the dose strip 450 is loaded into an inhaler having a plunger or other device moving perpendicularly to the dose strip 450, such as in the inhaler shown in U.S. Patent
35 Nos. 5,921,237 or 5,622,166. The back side 474 of the dose strip 450 is held in position in a track or other device. The tab 472, of the blister to be opened, is pushed upwardly from the bottom. As the base strip 452 is pre-cut through in the area underlying the cup 466,

and as the remaining areas of the base strip on the tab 472 are perforated, the tab 452 can be pushed or hinged upwardly with relatively low force. As this occurs, the cup layer 454 shears open, along the cut line 462. Typically the cup 466 will begin to shear at the apex of the cup or cone 466, with the shearing then moving outwardly to the circumference of the cup 466. The pharmaceutical powder contained within the cup can then fall out or be removed. The tab 472 is then moved back down so that the dose strip 450 is once again flat, on its top surface. The base strip 452 is sufficiently rigid so that the tab 472 does not deform significantly when it is pushed up to shear open a blister.

Turning to Figs. 52-55, a disk 502 having spaced apart blisters 504 containing a pharmaceutical 506, is provided within an inhaler 500 having a blister inverter device 512. The disk 502 has blisters formed in a blister layer 508. The pharmaceutical 506, typically a dry powder, is sealed in the blisters 504 between the blister layer 508 and a seal layer 510. Although the blisters 504 are shown on a round disk 502, they can also be placed on a straight, curved, or rolled strip, instead of a disk, by forming the features shown in a straight strip.

The inverter 512 includes a plunger 514 having a protruding end 518. The end 518 may be on the plunger itself, or it may be on a pin 520 slidably mounted within a collar 522, as shown in dashed lines in Fig. 53, with the collar 522 and the pin 520 together forming the plunger 514. The end 518 is preferably blunt or hemispherical, although other shapes between sharp and blunt may also be used. The inverter also includes a blister support 516, to support the perimeter or edges of a blister 504. The blister support 516 has a central opening 517 aligned under the end 518, and leading into a delivery chamber 524.

In use, the disk 502 is moved to bring a blister 504 directly over the opening 517 and under the end 518. The plunger 514 moves down and at least partially inverts the blister, turning it inside out. The blister layer 508 forming the top (preferably conical part) of the blister, is pushed from its upwardly projecting position, as shown in Fig. 53, into a downwardly position, as shown in Fig. 54. As this occurs, the seal layer 510 underlying the blister 504 shears or tears away around most of the circumference of the blister, releasing the pharmaceutical from the blister 504 into the chamber 524, for delivery to a patient. The seal layer underlying the blister remains attached to rest of the seal layer on the disk, at a retention sector, e.g., of about 30-150 degrees, and usually about 90 degrees. Consequently, after it is sheared out, the seal layer underlying the blister forms a flap 526 of shear layer material. To ensure that the shear layer forms a flap 526 and does not separate entirely from the disk, the plunger may be oriented at an acute angle to the disk, rather than approaching perpendicularly, as shown. Alternatively, the end or point 518 can be set at an angle, to shear out one side of the blister first, with the plunger movement stopped before the blister is sheared all around. Another technique of ensuring flap

formation is with the use of a shear/tear resistant segment 528, at one side of the blister 504, as shown in Fig. 55. The segment 528 is made of a material resistant to tearing or shearing, and it is bonded onto, or attached as overlay, at one side of the blister. The segment 528 prevents the seal layer above it from tearing, assuring that a flap (rather than a detached loose disk) will form as the dose is released.

In the alternative design shown in dashed lines in Fig 53, the collar 522 is first brought down against the disk 502, to clamp the disk in a fixed position, against the support 516, or to create a seal with the disk, to control air flow. Then the pin 520 is moved down to open the blister.

As shown in Figures 56 and 57, a carrier or plate 622 preferably includes a plurality of pivotable tabs 620. Each blister 624 is associated with a corresponding tab 620. Each tab 620 is adhered to one layer of the foil laminate 628 that makes up the blister 624. During operation, a first layer 630 of the foil laminate 628 is sheared out by its corresponding tab 620, via a blister opening mechanism in the inhaler 50. The pharmaceutical powder 626 then drops out of the blister and into a chute within the inhaler, as described in U.S. Patent No. 6,029,663.

The migration rate of water through the edges of the blister package is affected by several factors, including: 1.) the activity of the water inside the package relative to the activity of water outside the package; 2.) the nature of the barrier material the water must pass through (type of polymer, degree of cross-linking, hydrophobicity, etc.), and 3.) the distance, or sealed path length, that water must traverse from the edge of the seal the interior of the blister package. Factor 1 above is largely independent of the blister package design. Factor 2 above relates to the material of the blister package, rather than to the design of the blister package (i.e., its shape, features, dimensions, etc.). Factor 3 above can be directly related to the design of the blister package. However, simply increasing the sealed path length is not practical, as the blister package must be sufficiently compact to fit into or cooperate with an inhaler. The invention provides improved blister containers by increasing the sealed path length while maintaining compact blister container sizes.

Figure 58 illustrates a blister package 621 including a foil laminate 628 adhered to a carrier 622. The foil laminate 628 includes a first foil layer 630 and a second foil layer 632. Preferably the first and second foil layers 630, 632 are aluminum foil. An adhesive 634 is used to form the foil laminate 628 from the first and second foil layers 630, 632. The adhesive 634 is located external to the blister 624 containing the pharmaceutical powder 626. The adhesive 634 can be a glue-type adhesive, or, alternatively, an adhesive that is set using heat and/or pressure.

Preferably, as shown in Figure 58, the foil laminate 628 includes an outer edge 636 and an inner edge 638. The outer and inner edges 636, 638 are the points of termination of

the foil laminate 628 or blisterstock is adhered to the carrier 622 by adhesive 640. The blister package 621 may include, in an alternative embodiment, only an outer edge 636, for example as described more fully below and shown in Figure 74.

Referring still to Figure 58, the foil laminate 628 has a blister section 629 and a flap or folded section 633 folded back over the blister section 629 at a fold or hinge line 635. In this embodiment, the flaps 633 are folded over 180° or in a U-shape, to form a tortuous path or an elongated path in the laminate 628. The flaps 633 may be continuous or intermittent along the edges of the blister disk or strip. The flaps 633 may be bonded or attached to the blister section 629, or may simply be formed or folded over the blister section. The blister section 629 is preferably flat. The fold or bend line 635 preferably includes a radius, rather than a sharp edge, to reduce stresses on the laminate material. The radius may be large, e.g., from 1-50 times the thickness of the laminate, and preferably from 5-40 or 10-25 times the laminate thickness. Tortuous path here means a non-linear path such a curve, zigzag, U-turn, roll, coil, or similar shapes that impede the moisture transmission rate from the external environment to the blister 624.

Figure 59 shows the path length 42 (inner and outer) for the design in Figure 58. The path length is the distance from the centerline of the blister 624 to the outer edge 636 or inner edge 638. The path length is the distance that moisture must travel to reach the edge 625 of the blister via the interface (outermost or innermost) between the first layer 630 and second layer 632 of the foil laminate 628. Preferably, the path length 642 is equal to, or greater than 1.0 cm.

Figure 58 also illustrates, in dashed outline, the tab 620 and first foil layer 630 when the blister 624 is opened. When the first foil layer 630 is sheared away from the second foil layer 632 via tab 620, the pharmaceutical powder 626 moves out of the blister for delivery to a patient.

The blister package can also be provided in strip form, rather than disk form. Figure 60 illustrates a strip blister package 631 with the foil laminate 628 including a first or inner edge 638 and a second or outer edge 636. A first layer 630 of the foil laminate 628 is adhered to a carrier 622 via adhesive 640. A blister 624 is formed between the first and second foil layers 630, 632. Adhesive 634 is used to bond the first and second foil layers 630, 632 together. The foil laminate 628 is adhered to a carrier 622 via adhesive 640. In the strip form, the blister 624 may be broken by bursting, tearing or shearing. As shown in Figure 61, the path length 642 of each of the one or more blisters 624 to the outer edge 636 and inner edge 638 of the foil laminate 628 is at least 1.0 cm. The path length between the edges 636, 638 of the foil laminate 628 and the blister 624 is increased in comparison to conventional blister containers. The increased distance delays the entry

of moisture or water vapor into the pharmaceutical powder 626 contained with the blister 624.

Figure 62 illustrates another embodiment of a blister package 641 where the foil laminate 628 includes an outer edge 636 on a flap 633 rolled up against a flat blister section 637. A first foil layer 630 of the foil laminate 628 is adhered to a carrier 622 via adhesive 640. A blister 624 is formed between the first and second foil layers 630, 632. Adhesive 634 is used to bond the first and second foil layers 630, 632 together. A portion of the foil laminate 628, namely, the outer edge 636, as shown in Figure 62, contains a tortuous path. The tortuous path is in the shape of a roll. Figure 63 shows the path length 642 from the blister 624 to the outer edge 636. Preferably, the path length 642 is equal to, or greater than 1.0 cm.

Figure 64 illustrates another embodiment of a blister package 651 having an inner edge 638 and an outer edge 636 that is wrapped into a rolled or coil shaped structure. A first foil layer 630 of the foil laminate 628 is adhered to a carrier 622 via adhesive 640. A blister 624 is formed between the first and second foil layers 630, 632. Adhesive 634 is used to bond the first and second foil layers 630, 632 together. A portion of the foil laminate 628, namely, the outer edge 636 as shown in Figure 64, contains a tortuous path. The tortuous path is in the shape of a coil. Figure 65 shows the path length 642 from the blister 624 to the inner edge 638 and the outer edge 636. Preferably, the path length 642 for both the inner and outer edges 638, 636 is equal to, or greater than 1.0 cm.

Figure 66 illustrates yet another embodiment of a blister package 661 with a first foil layer 630 of foil laminate 628 adhered to a carrier 622 via adhesive 640. A blister 624 is formed between the first and second foil layers 630, 632. Adhesive 634 is used to bond the first and second foil layers 630, 632 together. In this embodiment, a flap portion 643 of the foil laminate 628 near the inner edge 628 and outer edge 636 has a wavy or zigzag shaped structure. The tortuous path is thus in the shape of a zigzag, having multiple bend or fold lines 645. Figure 67 illustrates the path length 642 from the blister 624 to the inner edge 638 and outer edge 636. Preferably, the path length 642 for both the inner and outer edges 638, 636 is equal to, or greater than 1.0 cm.

Figure 68 illustrates still another embodiment of a blister package 671 with a first foil layer 630 of foil laminate 628 optionally adhered to a carrier 622 via adhesive 640. Blisters 624 are formed between the first and second foil layers 630, 632. Adhesive 634 is used to bond the first and second foil layers 630, 632 together. In this embodiment, a flap portion 653 of the foil laminate 628 includes a 90° bend at bend line 655. The bend provides the blister package 671 with a cup shaped structure. Figure 69 illustrates the path length from a representative blister 624 to the inner edge 638 and outer edge 636. Preferably, the path length 642 for both the inner and outer edges 638, 636 is equal to, or

greater than 1.0 cm. The center hole shown in Fig. 68 may be omitted to provide for a longer path length 642.

Figure 70 illustrates another blister package 681 including a plurality of blisters 624 formed between a first foil layer 630 and a second foil layer 632. Adhesive 634 is used to bond the first and second foil layers 630, 632 together. The first layer of foil laminate 630 is optionally adhered to a carrier via adhesive (the carrier and adhesive are blocked from view in Figure 70 by the foil laminate 628). The foil laminate 628 includes individual panels 644 preferably formed by making radial cuts in the foil laminate 628. During assembly of the blister package 681, the panels 644 are folded over at a bend line 665 as shown by the dashed lines AA. Figure 71 illustrates the path length 642 from the blister 624 to the inner edge 638 and outer edge 636 (inner and outer). In this embodiment, the path length 642 for the inner edge 638 and outer edge 636 is taken along the radius or radial direction of the blister package 681. Preferably, the path length 642 for both the inner and outer edges 638, 636 is equal to, or greater than 1.0 cm.

Figure 72 illustrates another embodiment of a blister package 691 including a plurality of blisters 624 formed between a first foil layer 630 and a second foil layer 632. Adhesive 634 is used to bond the first and second foil layers 630, 632 together. The first layer of foil laminate 630 is optionally adhered to a ring-shaped carrier via adhesive (the carrier and adhesive are blocked from view in Figure 72 by the foil laminate 628). The foil laminate 628 includes panels 644 on the outside and inside of the blister package 691. During assembly of the blister package 691, the panels 644 are folded over at a bend line 675 as shown by the dashed lines BB. Figure 73 illustrates the path length 642 from the blister 624 to the inner edge 638 and outer edge 636. In this embodiment, the path length 642 for the inner edge 638 and outer edge 636 is taken along the radius or radial direction of the blister package 691. Preferably, the path length 642 for both the inner and outer edges 638, 636 is equal to, or greater than 1.0 cm.

Figure 74 illustrates another embodiment of a blister package 701 is analogous to Figures 70 and 72 except that the blister package 701 includes a solid interior portion. Hence, there is no inner edge 638 to the foil laminate 628. Instead, the foil laminate only has an outer edge 636.

The containers shown and described increase the seal path length to improve the stability of powder pharmaceutical contents, by delaying the passage of atmospheric water vapor into the blister containers. Thus, the shelf life is prolonged. Secondary packaging may also not be necessary. The novel geometries provided also maintain the containers in a compact form, by the folding, rolling, undulating, etc. The various carriers described may be omitted to provide containers formed only of foils or laminate constructions. Heat and pressure techniques may be used in place of adhesives.

Of course, any of the designs shown above can also be used in a single dose unit, strip, disk, etc., having a single blister.

Claims

1. A dose strip for use with a powder inhaler, comprising:
a base strip having a plurality of spaced apart blisters;
a pharmaceutical powder in the blisters;
5 a lid strip attached over the base strip and sealing the pharmaceutical powder within the blisters;
a plurality of lid tabs attached to the lid strip, with a peel tab located substantially over each blister; and
a peel strip attached to each peel tab.
- 10 2. The dose strip of claim 1 wherein the base strip and the lid strip comprise a metal foil.
3. The dose strip of claim 1 wherein the peel strip comprises a string or a wire.
4. The dose strip of claim 1 wherein the blisters are evenly spaced apart along
15 the length of the dose strip.
5. The dose strip of claim 1 wherein the lid tabs are spaced apart from each other and are on opposite sides of a joining segment of the dose strip.
6. The dose strip of claim 1 wherein the attachment between the peel strip and the lid tabs and the lid strip is stronger than the shear strength of the lid strip, so that
20 pulling on the peel strip causes the lid strip over or around a blister to shear open to allow release of the pharmaceutical powder in the blister.
7. The dose strip of claim 1 wherein the dose strip contains a multiplicity of blisters and the dose strip is coiled into a spiral configuration.
8. A dose strip for use with a dry powder pharmaceutical inhaler, comprising:
25 a base strip having a plurality of spaced apart loop tabs; and
a drum attached to each of the loop tabs, the drum having a hollow body containing a pharmaceutical powder, with the ends of the hollow body sealed by the loop tabs.

9. The dose strip of claim 8 wherein the drum is movable from a first position adjacent to the base strip to an extended position away from the base, with the hollow body sealed by the loop tabs when the drum is in the first position, and with the hollow body unsealed and open when the drum is in the extended position.

5 10. The dose strip of claim 9 wherein the dose strip is formed into a ring.

11. A dry powder inhaler comprising:
a housing having a mixing chamber;
a dose strip within the housing;
a plurality of drums attached to the dose strip
10 a carrier sealed within each drum, each carrier having an opening containing a dose of a pharmaceutical powder;
a plunger in the housing adjacent to the mixing chamber;
means for advancing the dose strip to bring successive drums on the dose strip into alignment with the plunger; and
15 means for actuating the plunger to drive the carrier out of the drum.

12. A dry powder inhaler comprising:
a housing;
a dose strip within the housing;
the dose strip including a plurality of blisters on a head plate, each blister
20 containing a pharmaceutical powder, a seal over the blisters, and a plunger attached to the seal; and
a button associated with each blister, and with each button movable from a first position above the blister wherein the blister is sealed, to a second position wherein the button moves the plunger away from the head plate causing the seal to tear away from the
25 blister, to allow the pharmaceutical powder to be inhaled.

13. The dry powder inhaler of claim 12 further comprising an anvil on the button adapted to crush the blister as the button moves into the second position.

14. A method for opening a blister containing a dry powder pharmaceutical, comprising:
30 aligning a blister having a top layer and a bottom layer, under a plunger;
supporting the blister around its edges;

moving the plunger into contact with the top layer of the blister and pushing the top layer of the blister downwardly;
creating an opening in the blister by separating the bottom layer from the top layer;
and
5 removing the dry powder pharmaceutical from the blister via the opening.

15. The method of claim 14 wherein the blister is conical, hemispherical, or oval.

16. The method of claim 14 further comprising the step of holding a section of the bottom layer onto the top layer, thereby preventing the bottom layer from separating
10 entirely from the top layer.

17. The method of claim 16 further comprising the step of holding the section of the bottom layer onto the top layer by providing shear resistant layer between them at the section.

18. The method of claim 14 further comprising the step of holding the blister
15 in place by supporting a perimeter of the bottom layer on a blister support, and pressing the blister against the blister support with the plunger.

19. A dry powder inhaler comprising:
a blister support for supporting a blister at the perimeter of the blister;
a blister inverter including a plunger having a protruding tip and a plunger driver
20 for moving the plunger towards and away from the blister; and
a powder chamber under the blister support for catching powder released from the blister.

20. The dry powder inhaler of claim 19 wherein the plunger tip has a radius greater than the radius of the blister.

21. The dry powder inhaler of claim 20 wherein the blister and plunger tip are
25 conical.

22. A dose strip containing individual doses of a pharmaceutical comprising:
a first layer having a recess;
a cut line severing the recess;

a second layer in the recess;
a third layer over the second layer;
a dose of a pharmaceutical between the second layer and the first layer.

5 23. A dose strip containing individual doses of a pharmaceutical comprising:
a first layer having a plurality of spaced apart recesses:
a cut line through each of the recesses severing the first layer at each of the
recesses into a first section and a second section;
a shearable second layer attached to the first layer, with the second layer including
a plurality of spaced apart blisters, with one blister in each of the recesses of the first layer;
10 a pharmaceutical dose in each of the blisters;
a third layer attached to the second layer, with the pharmaceutical dose sealed
between the second layer and the third layer.

24. The dose strip of claim 23 further comprising a perforation in the first layer
extending between each pair of adjacent recesses.

15 25. The dose strip of claim 23 further comprising a cutout in the first, second,
and third layers, between adjacent blisters, with the cutouts dividing the dose strip into a
plurality of individual dose segments.

20 26. The dose strip of claim 23 wherein the first section of each recess is
pivotable relative to the second section thereof, to shear open the blister in the recess and
release the pharmaceutical dose.

27. An inhaler comprising:
a dose strip having spaced apart blisters each containing a pharmaceutical powder;
an angled roller in the inhaler, the angled roller having a first angled roller surface
and a second angled roller surface positioned at an angle to the first angled roller surface;
25 a first side roller having a first side roller surface parallel to the first angled roller
surface;
a second side roller having a second side roller surface parallel to the second
angled roller surface, with the dose strip extending between the angled roller and the first
and second side rollers; and
30 an advancing mechanism in the inhaler engaging the dose strip, for incrementally
advancing the dose strip.

28. The inhaler of claim 27 further comprising a knife adjacent to the angled roller and positioned to sever the blisters on the dose strip, as the dose strip advances.

29. The inhaler of claim 28 wherein the blisters are elongated.

5 30. A dose strip comprising:
a base strip having a plurality of spaced apart cups;
a pharmaceutical dose in each of the cups; and
a seal strip having a plurality of seal plates, with each seal plate extending into and engaging a cup on the base strip.

10 31. A dose strip comprising:
a base strip having a plurality of spaced apart cups;
a pharmaceutical dose in each of the cups;
a plurality of lids, with each lid associated with a cup, each lid including a seal plate extending into and engaging one of the cups, and each lid including a lift tab; and
a hinge attached to each of the lids and to the base strip.

15 32. The dose strip of claim 31 wherein the base strip, lids and hinges are molded as an integral unit.

33. The dose strip of claim 31 wherein the base strip, lids and hinges are formed from a metal foil.

20 34. A container for a dry powder pharmaceutical comprising:
a foil laminate including a first layer and a second layer adhered to each other and terminating at a first laminate edge;
one or more blisters formed between the first and second layers on a blister section of the foil laminate;
a dose of a dry powder pharmaceutical contained in the blister;
25 where the distance from the blister to the laminate edge of the foil laminate is at least 1.0 cm and where the blister is separated from the laminate edge by at least one first bend line.

35. The container of claim 34 with the foil laminate further including at least one first flap section attached to the blister section at the first bend line.

36. The container of claim 35, wherein the first flap section is parallel to the blister section.

37. The container of claim 35 where the first flap section is perpendicular to the blister section.

5 38. The container of claim 35 with the first flap section including at least one second flap section joined to the first flap section at a second bend line.

39. The container of claim 35, wherein the first flap section is cup-shaped.

40. The container of claim 34 further including a carrier bonded onto the foil laminate.

10 41. The container of claim 34, wherein the first flap section is roll- shaped.

42. A container for pharmaceuticals comprising:
a carrier;

a foil laminate containing a first and second layer of metal foil, with the second layer of metal foil adhered to the carrier, the foil laminate terminating in an outer edge and
15 an inner edge;

one or more blisters located between the first and second layers of metal foil for the storage of the pharmaceutical; and

wherein the path length of each of the one or more blisters to the outer edge and inner edge of the foil laminate is at least 1.0 cm and wherein a portion of the foil laminate
20 between the one or more blisters and the outer edge of the foil laminate is tortuously shaped.

43. The container of claim 42, wherein the two layers of foil are aluminum.

44. The container of claim 42, wherein the tortuously shaped region includes a U-turn.

25 45. The container of claim 42, wherein the tortuously shaped region is in the shape of a zigzag pattern.

46. The container of claim 42, wherein the tortuously shaped region is in the shape of a coil.

47. The container of claim 42, wherein the tortuously shaped region is in the shape of a cup.

5 48. The container of claim 42, wherein the tortuously shaped region includes at least one bend of at least 90 °.

49. The container of claim 42, wherein the tortuously shaped region is in the shape of a roll.

10 50. A container for pharmaceuticals comprising:
a carrier;
a foil laminate containing a first and second layer of metal foil, one of the a first and second layers of metal foil being adhered to the carrier, the foil laminate terminating in an outer edge and an inner edge;
one or more blisters located between the a first and second layers of metal foil for
15 the storage of the pharmaceutical; and
wherein the path length of each of the one or more blisters to the outer edge and inner edge of the foil laminate is at least 1.0 cm and wherein a portion of the region of the foil laminate between each one or more blisters and the inner edge of the foil laminate is tortuously shaped.

20 51. The container of claim 50, wherein the two layers of foil are aluminum.

52. The container of claim 50, wherein the tortuously shaped region includes a U-turn.

53. The container of claim 50, wherein the tortuously shaped region is in the shape of a zigzag pattern.

25 54. The container of claim 50, wherein the tortuously shaped region is in the shape of a coil.

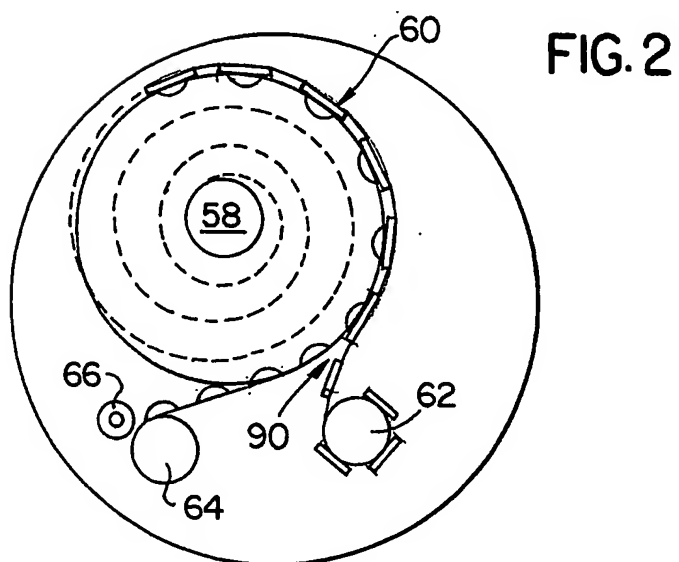
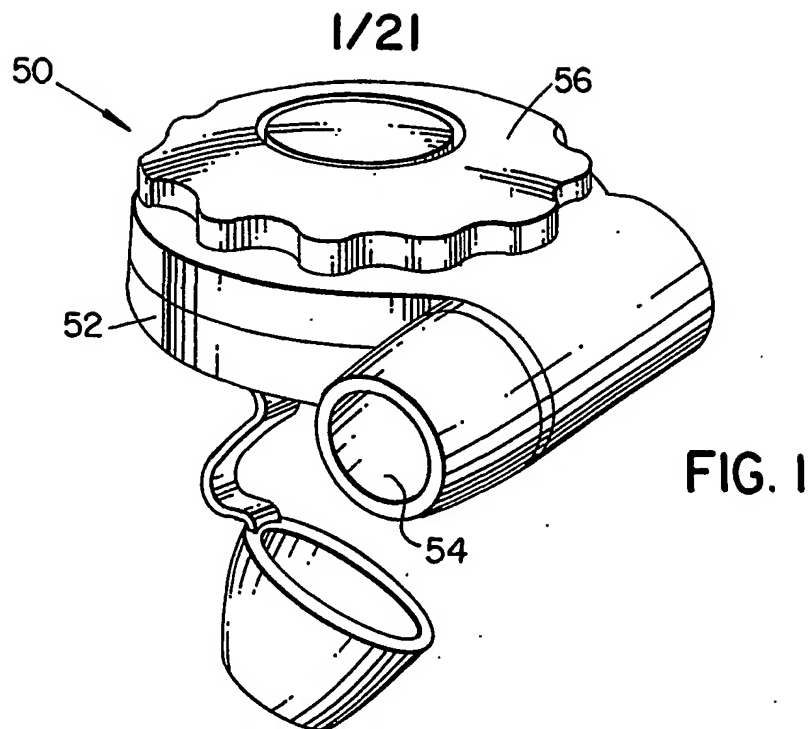
55. The container of claim 50, wherein the tortuously shaped region is in the shape of a cup.

56. The container of claim 50, wherein the tortuously shaped region includes at least one bend of at least 90 °.

57. The container of claim 50, wherein the tortuously shaped region is in the shape of a roll.

5 58. A method of making a carrier for pharmaceuticals comprising:
providing a carrier;
providing a foil laminate having one or more blisters containing the pharmaceutical compound therein, the foil laminate containing a first and second layer of metal foil and further having an outer edge, wherein the path length of each of the one or more blisters to
10 the outer edge of the foil laminate is at least 1.0 cm;
affixing one of the a first and second layers of the foil laminate to the carrier;
forming a tortuous pathway between the one or more blisters and the outer edge of the foil laminate.

15 59. A method of making a carrier for pharmaceuticals comprising:
providing a carrier;
providing a foil laminate having one or more blisters containing the pharmaceutical compound therein, the foil laminate containing a first and second layer of metal foil and further having an inner edge and an outer edge, wherein the path length of each of the one or more blisters to the outer edge and inner edge of the foil laminate is at least 1.0 cm;
20 affixing one of the a first and second layers of the foil laminate to the carrier;
forming a tortuous pathway between the one or more blisters and the inner edge of the foil laminate.



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FIG. 3

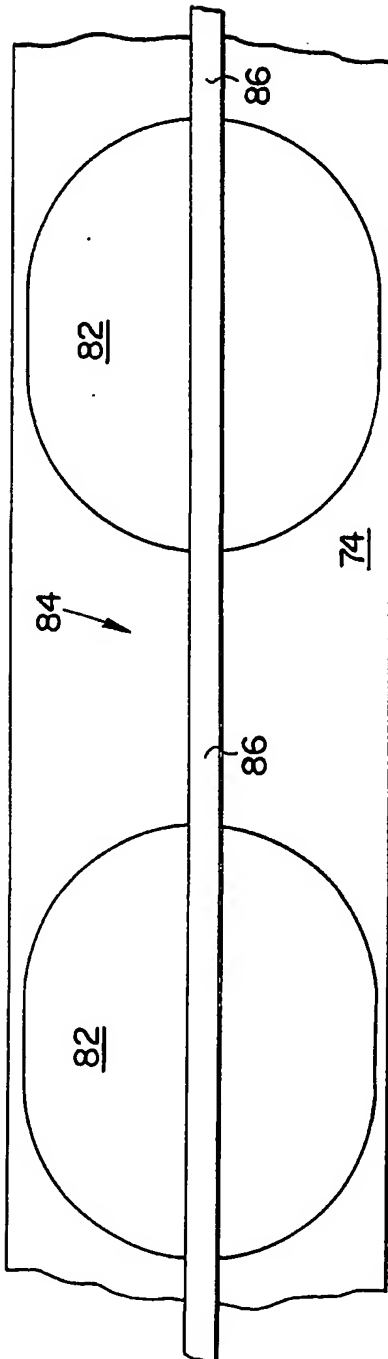


FIG. 4

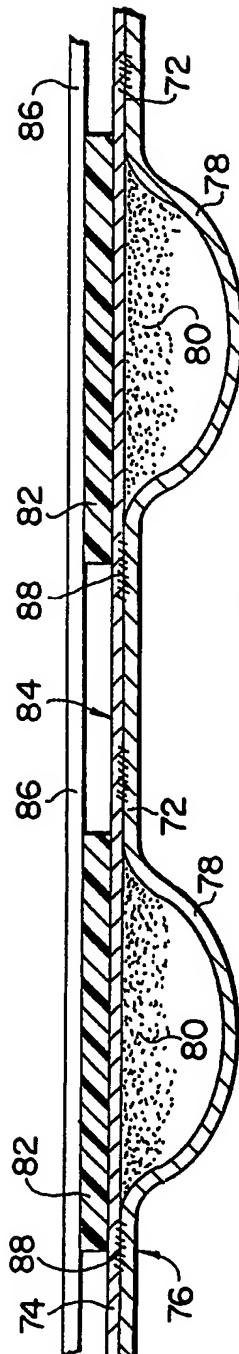


FIG. 5

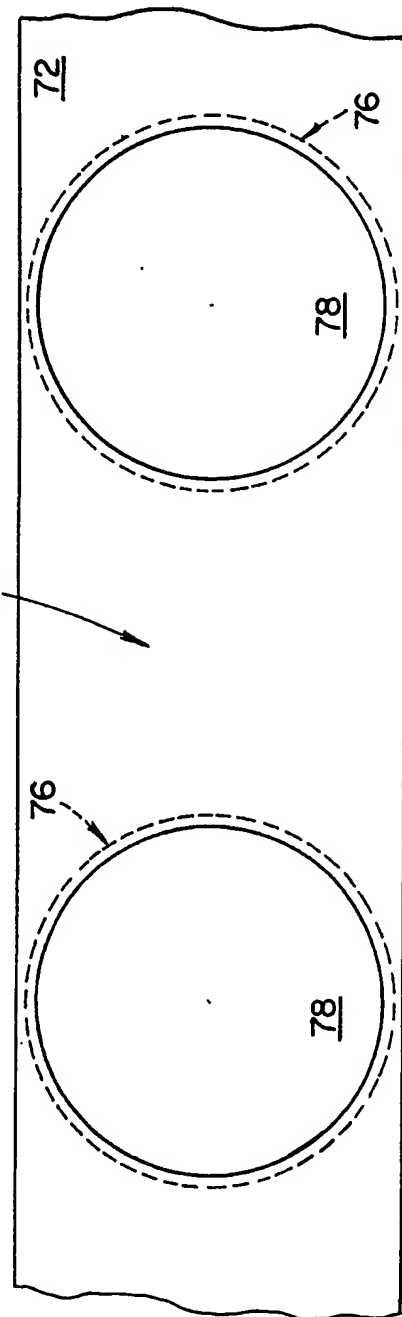


FIG. 6 3/21

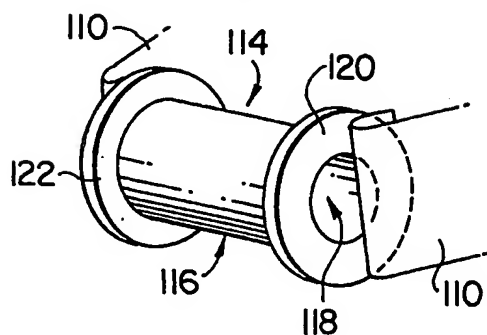


FIG. 7

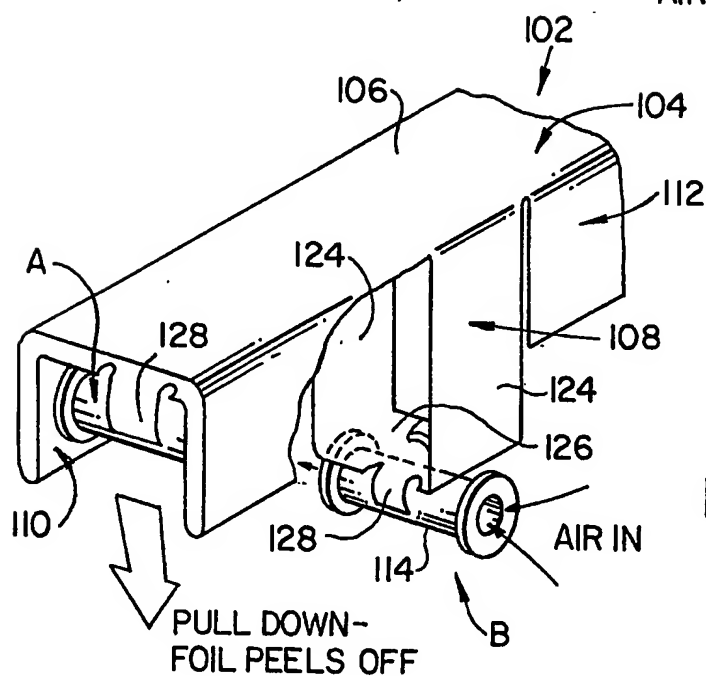
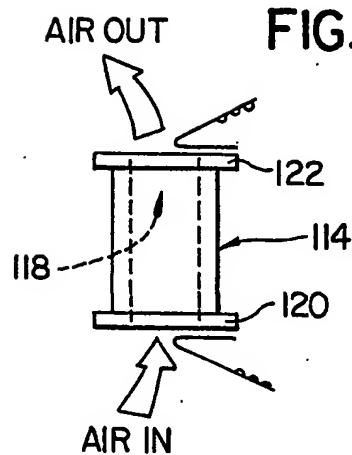


FIG. 8

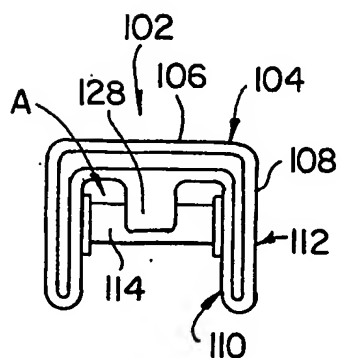


FIG. 8A

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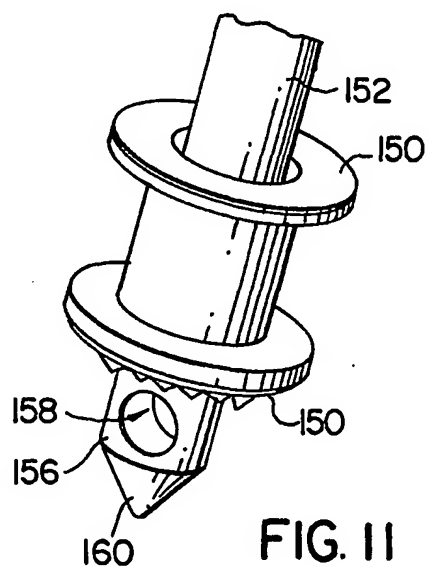
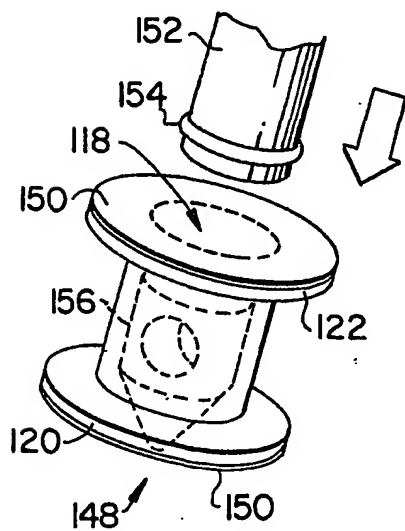
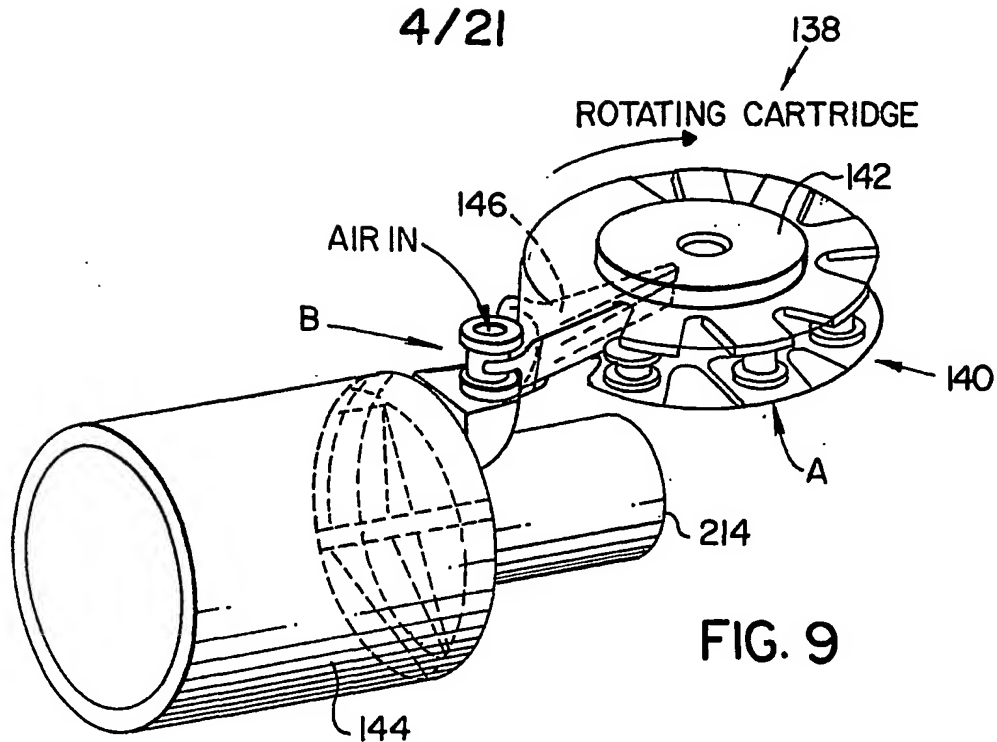


FIG. 12 5/21

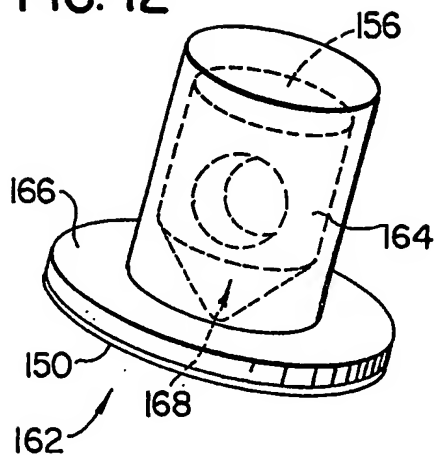


FIG. 13

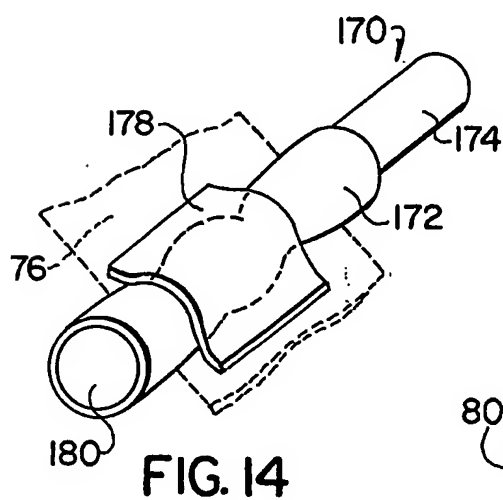
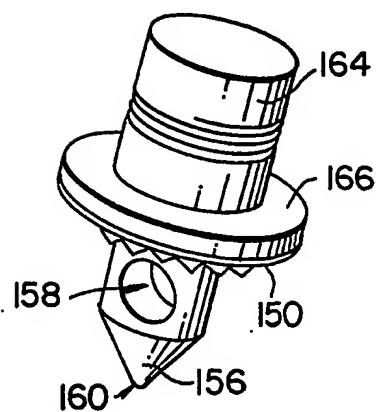


FIG. 14

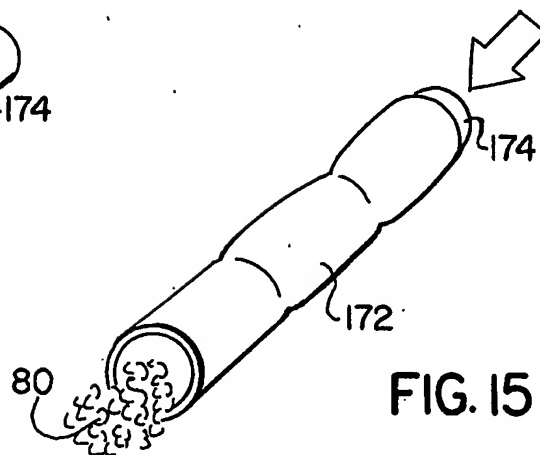


FIG. 15

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FIG. 16

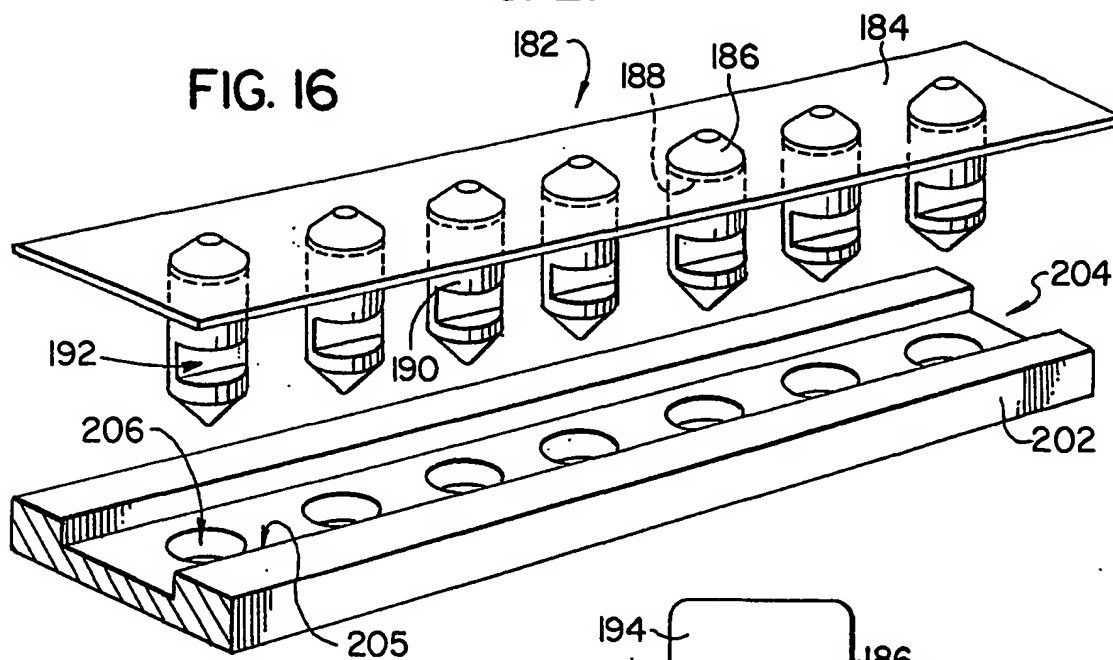


FIG. 17

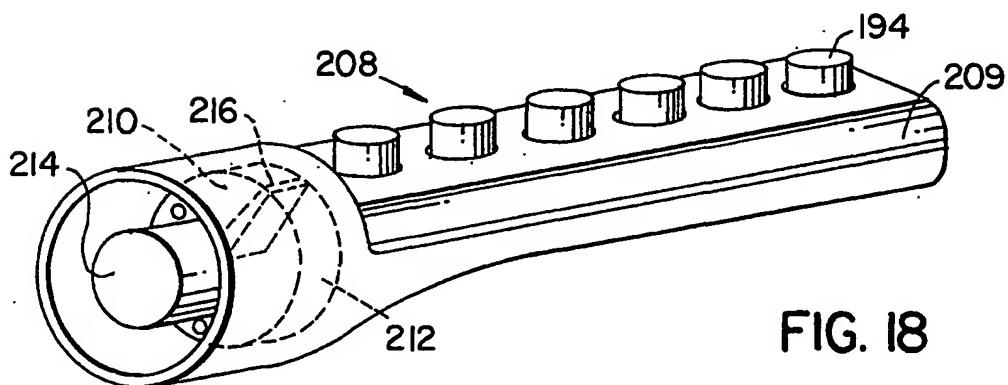
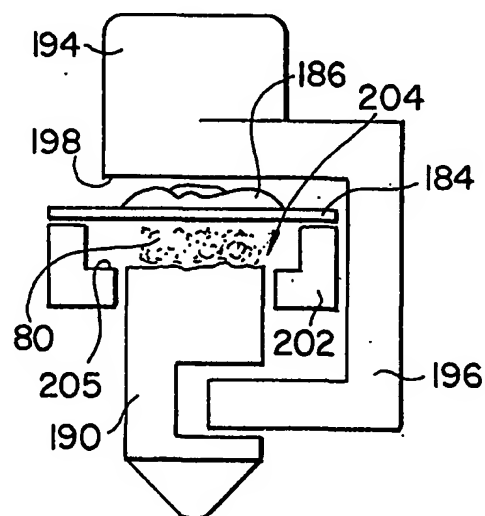


FIG. 18

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FIG. 19

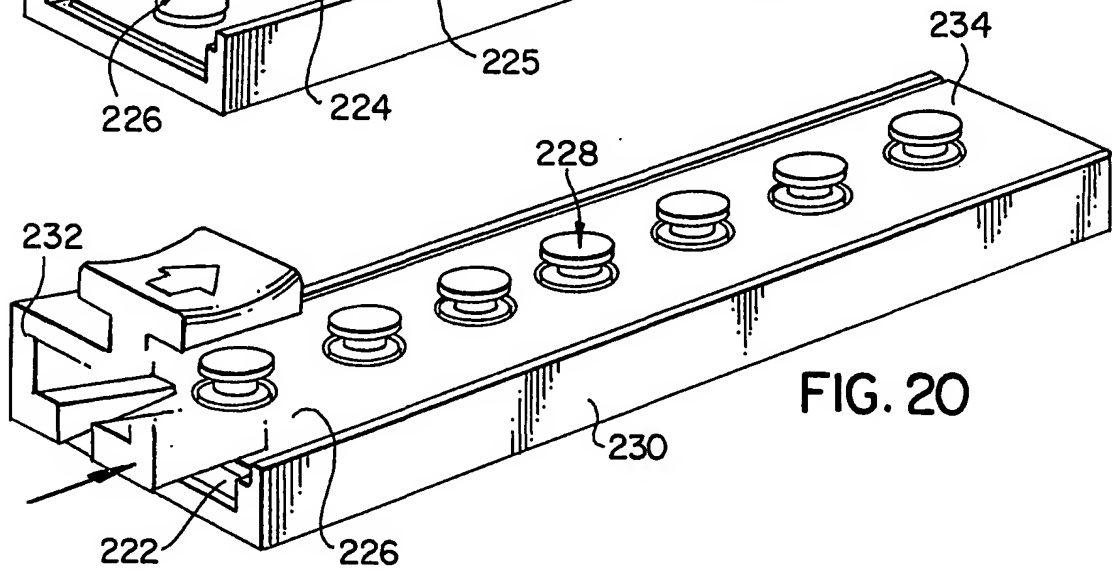
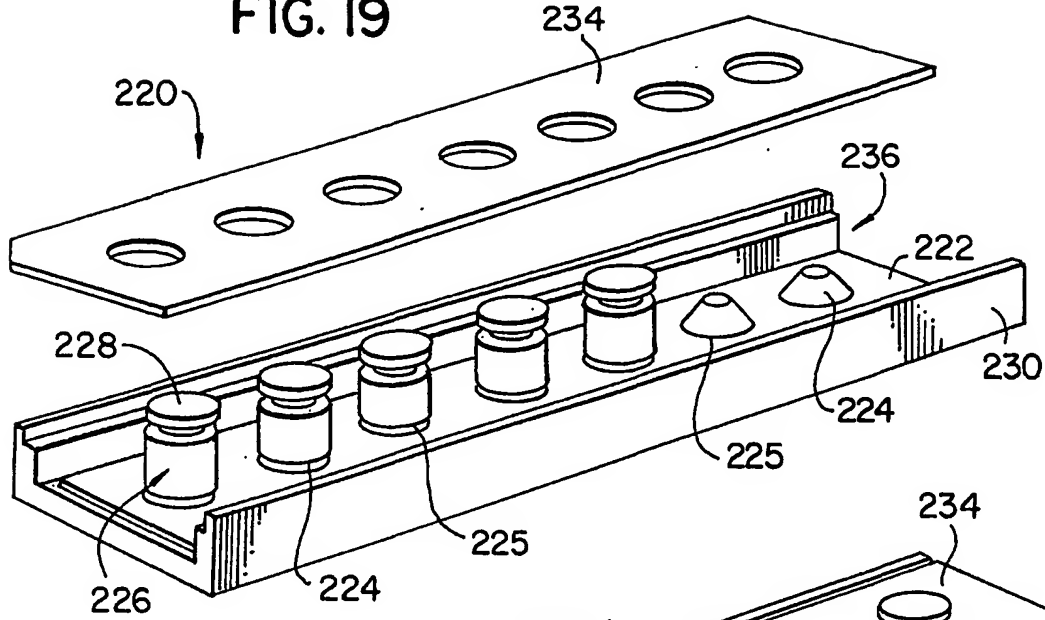


FIG. 20

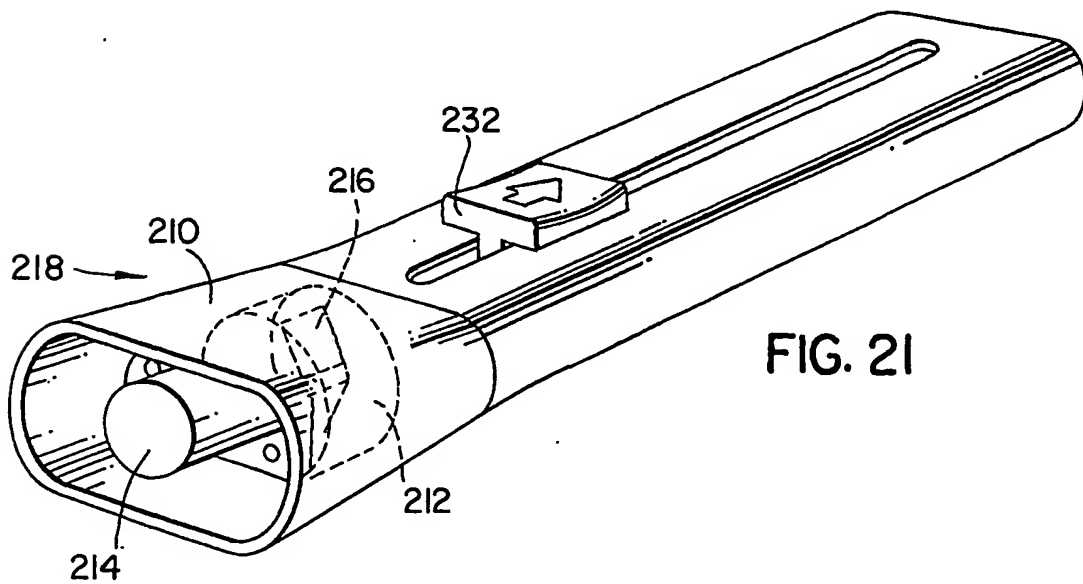


FIG. 21

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FIG. 22

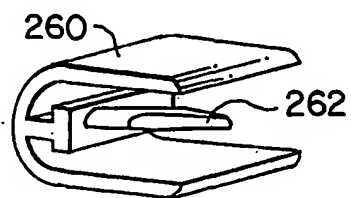
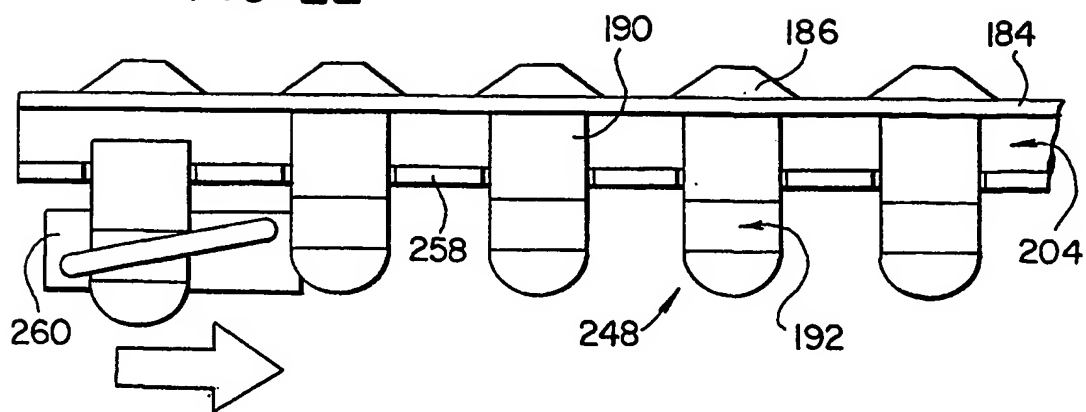


FIG. 23

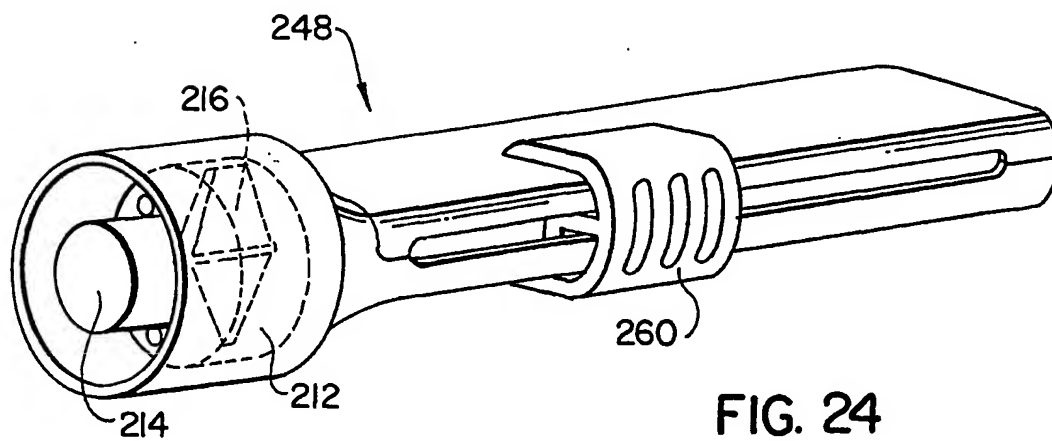
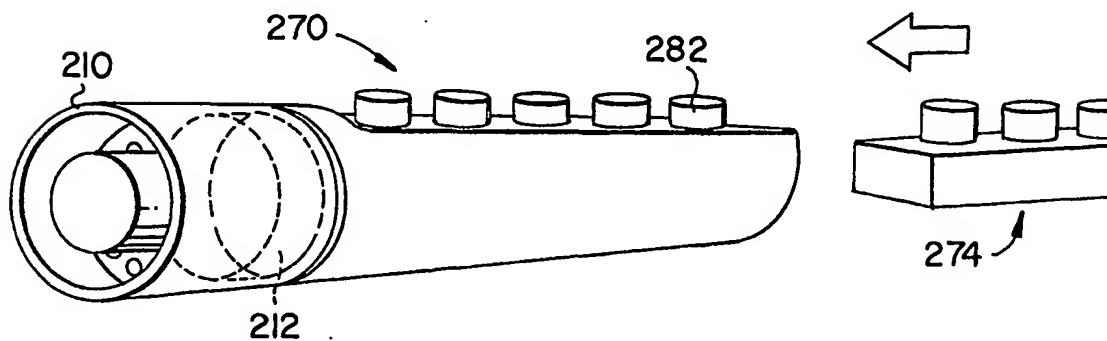
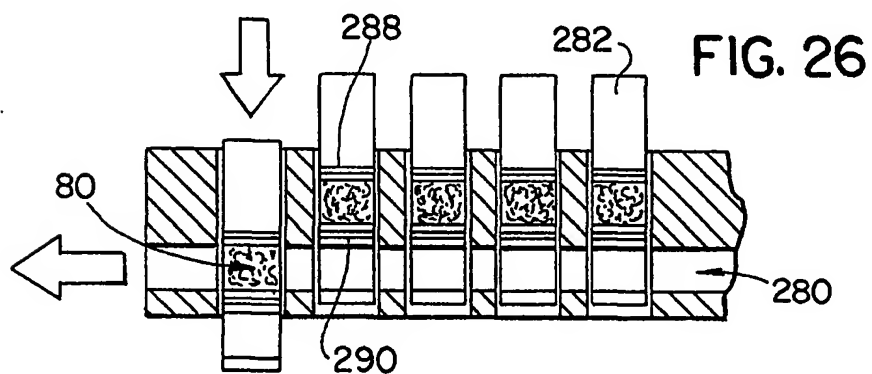
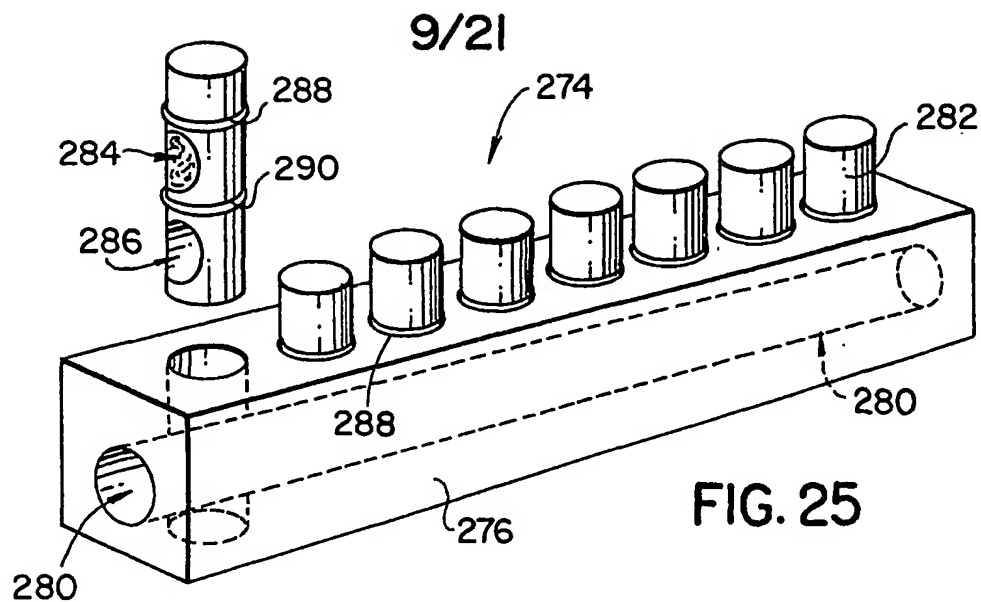


FIG. 24



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FIG. 30

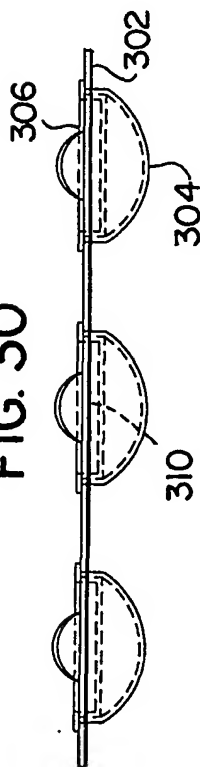


FIG. 31

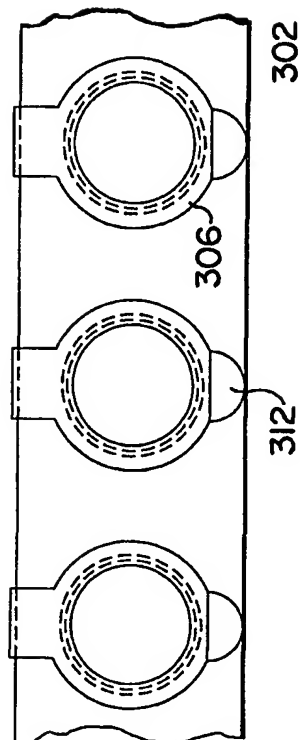
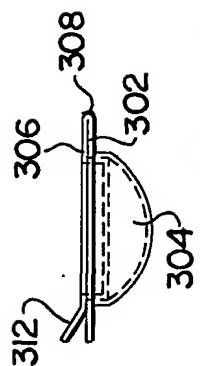


FIG. 29

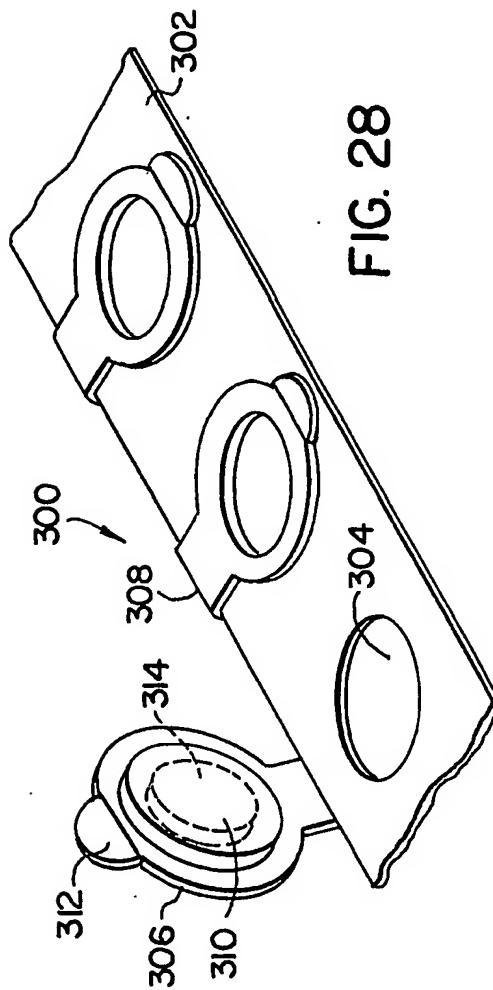
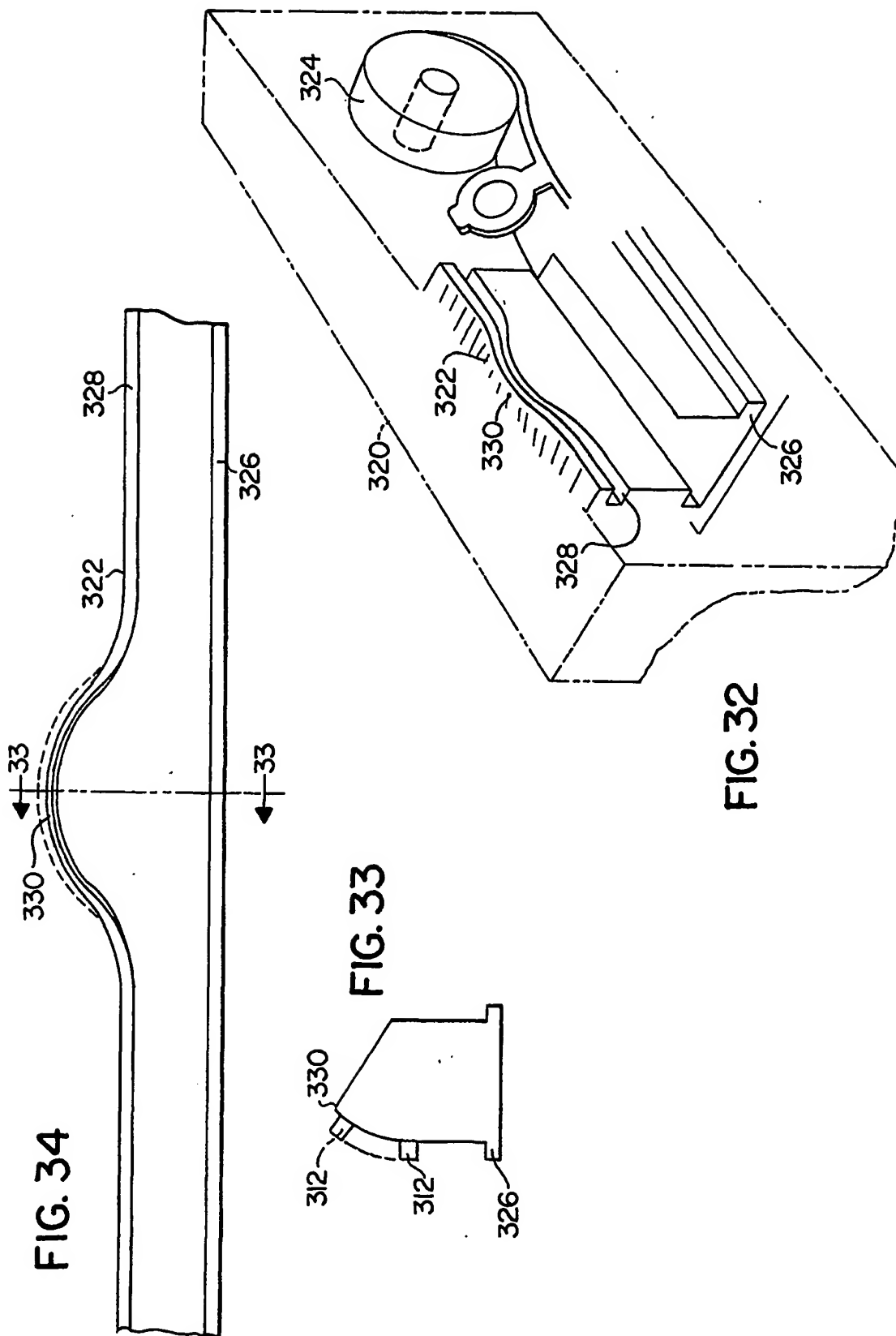


FIG. 28

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FIG. 37

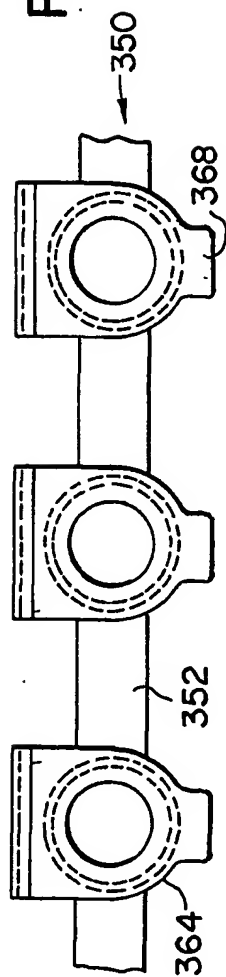


FIG. 38

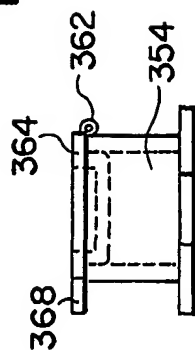


FIG. 36

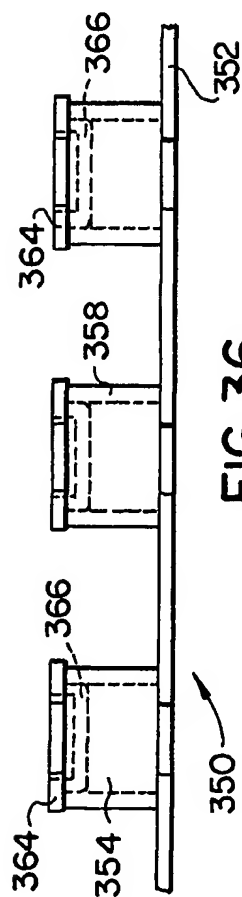


FIG. 35

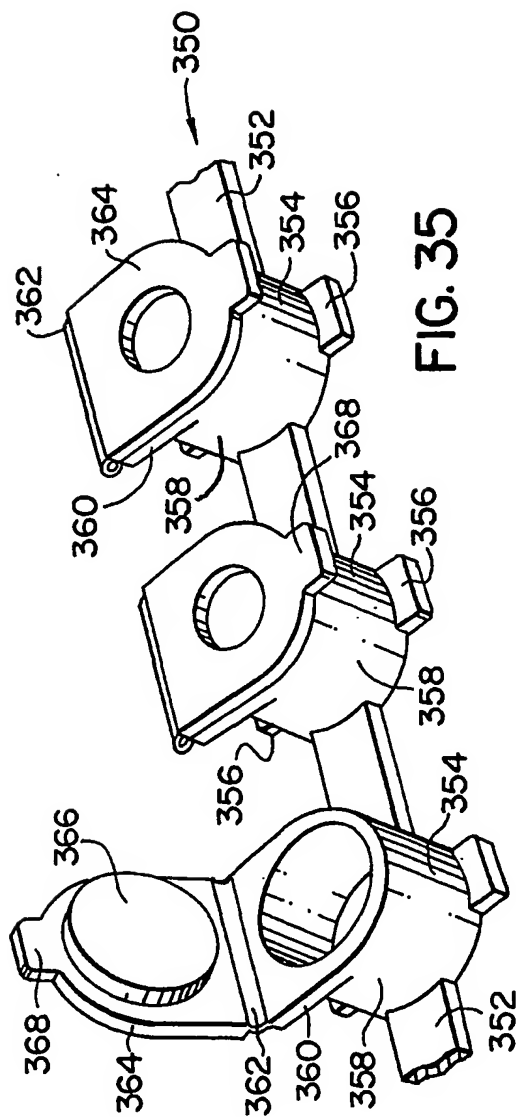


FIG. 41

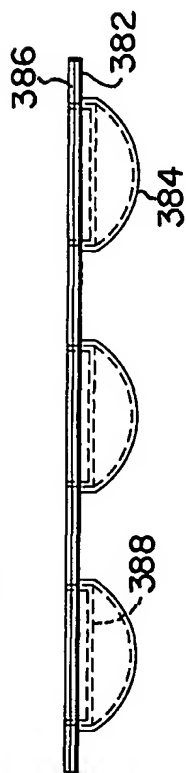


FIG. 42

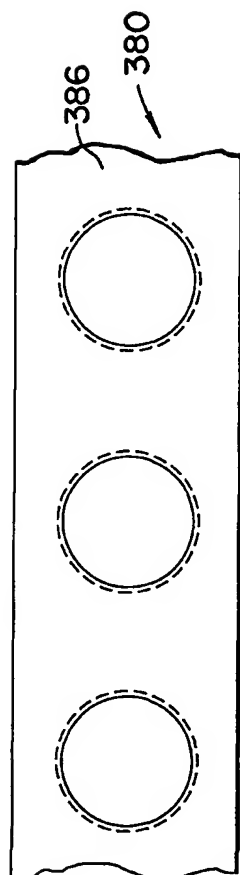
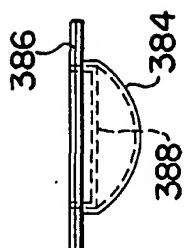


FIG. 40

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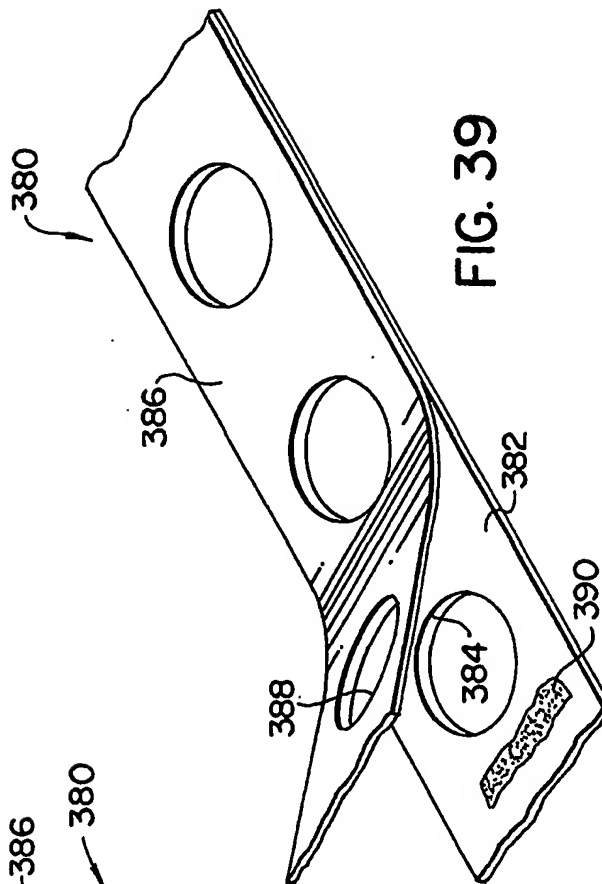


FIG. 39

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FIG. 46

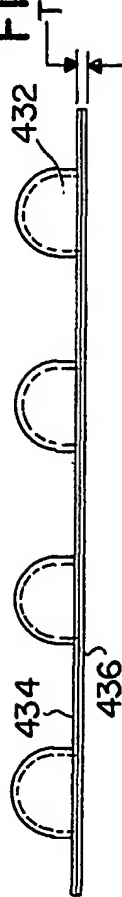


FIG. 44

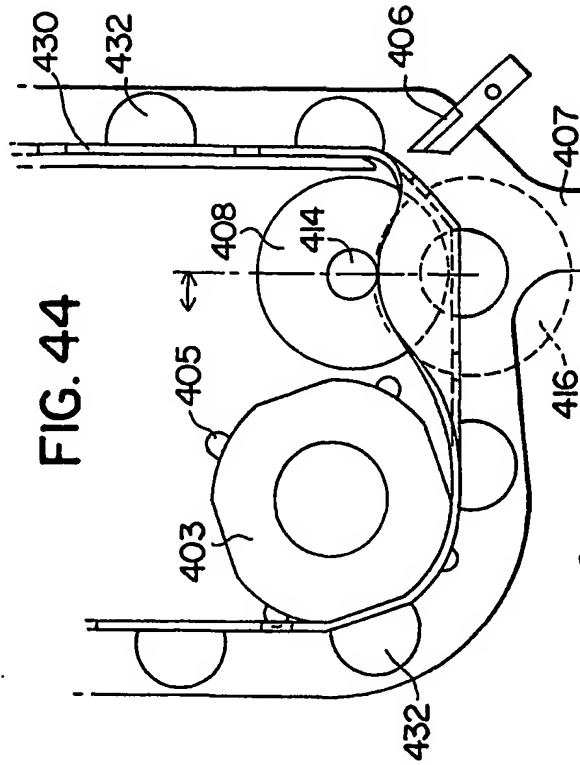


FIG. 45

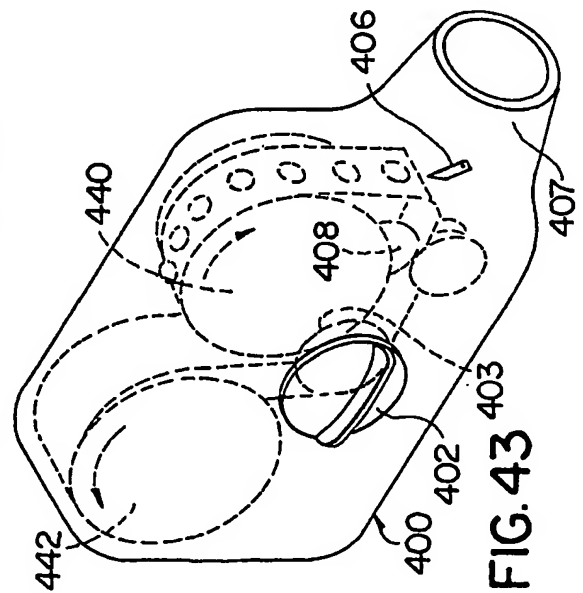
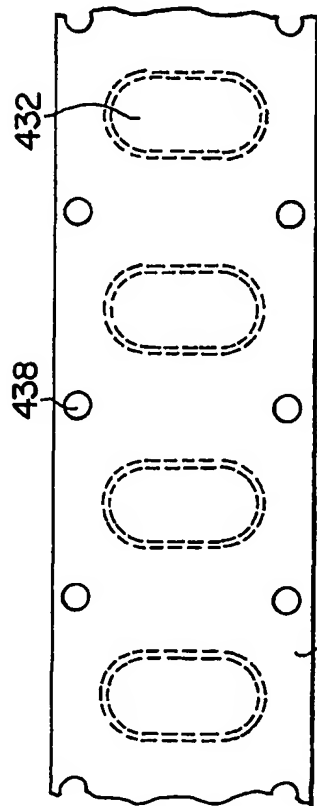
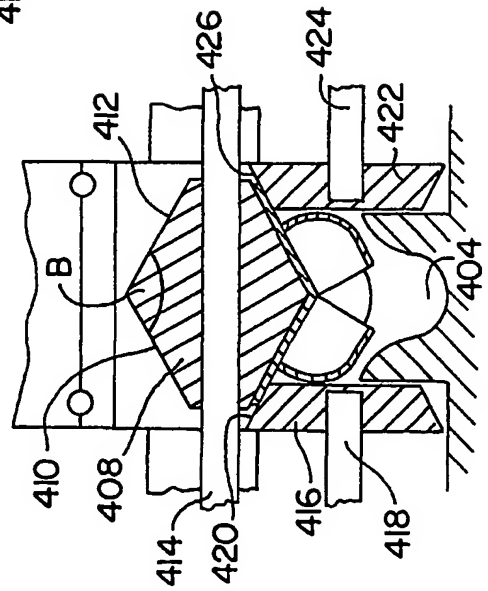


FIG. 47



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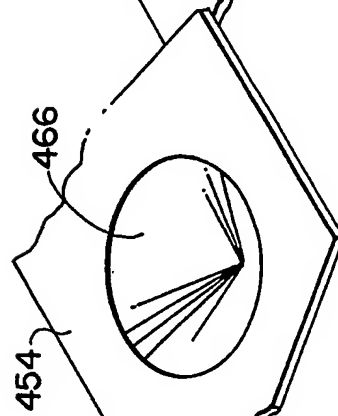
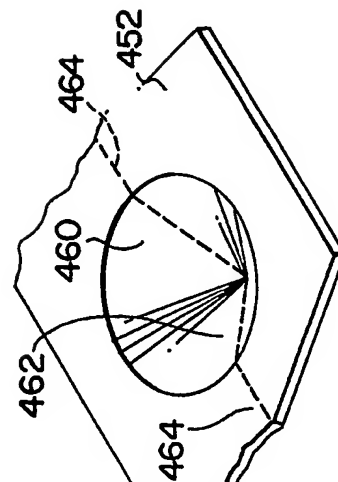
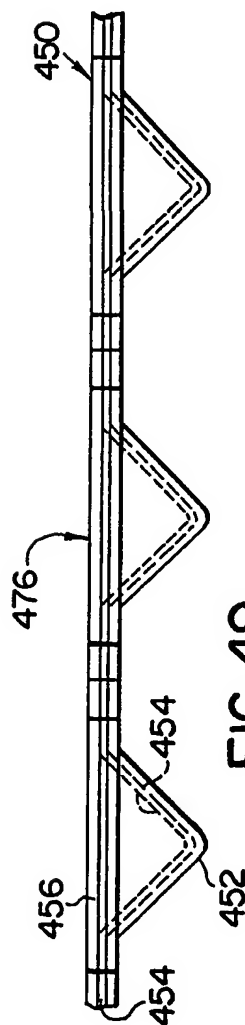
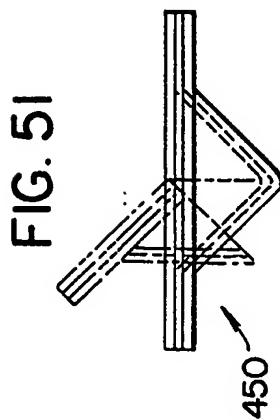
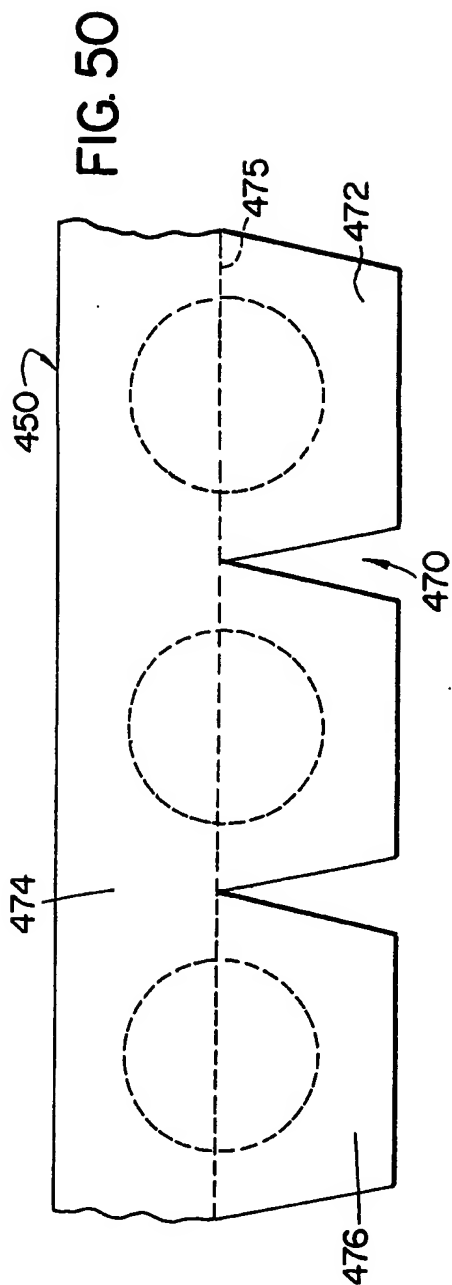


FIG. 48

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FIG. 53

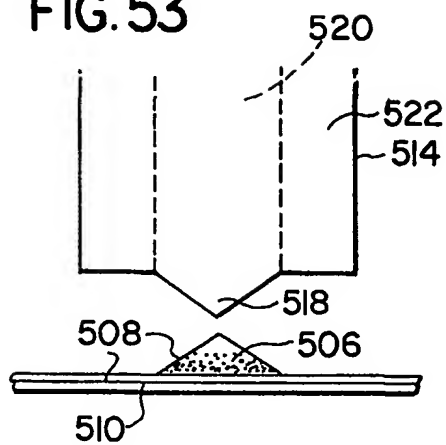


FIG. 54

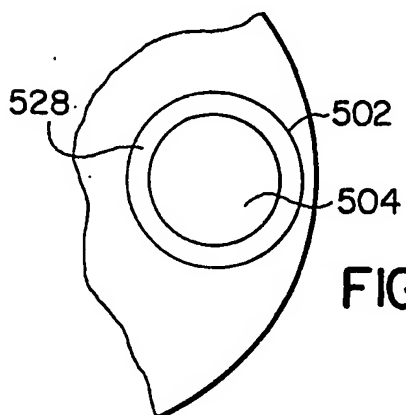
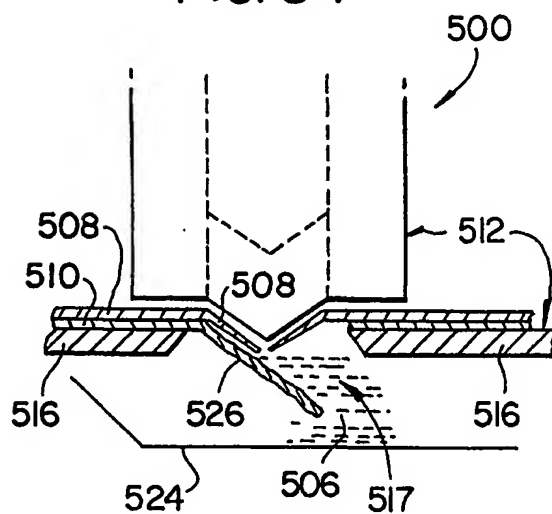
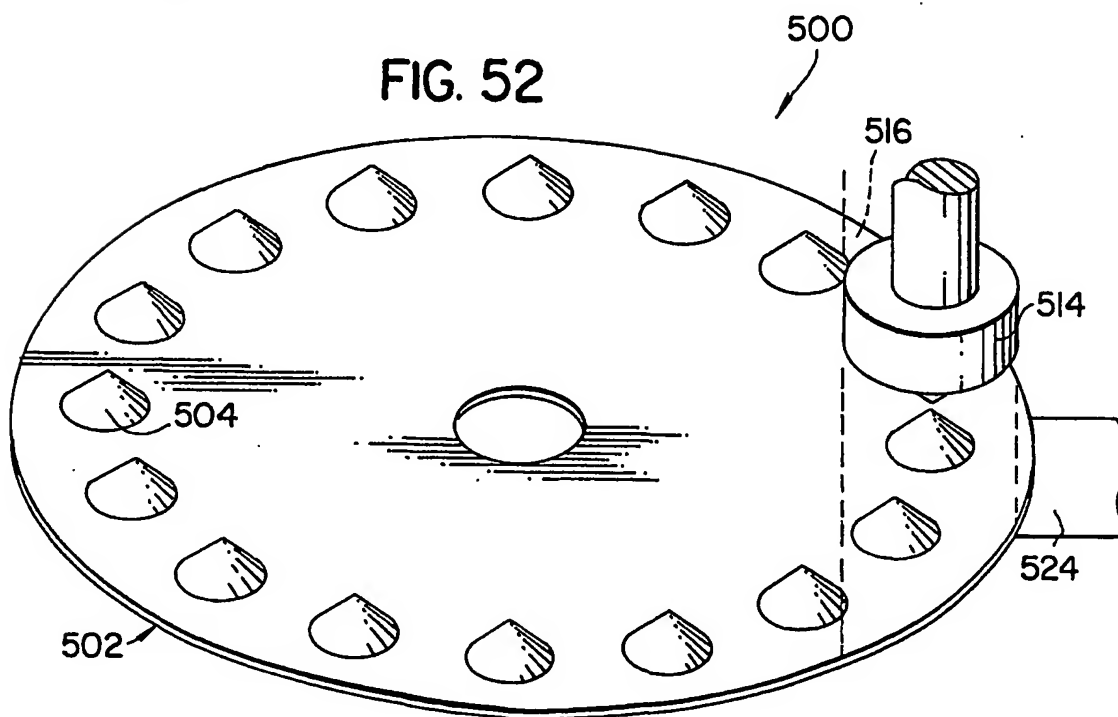


FIG. 55

FIG. 52



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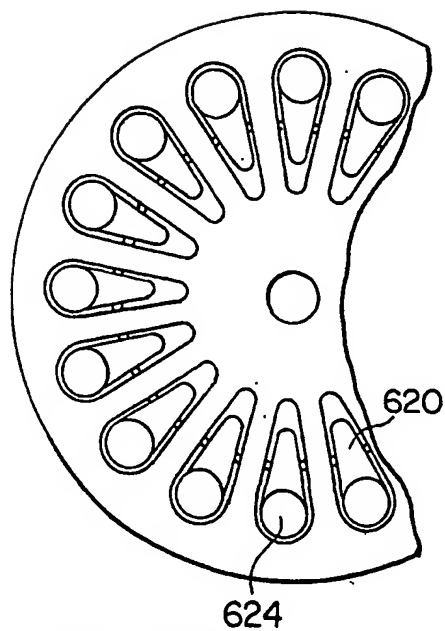


FIG. 56

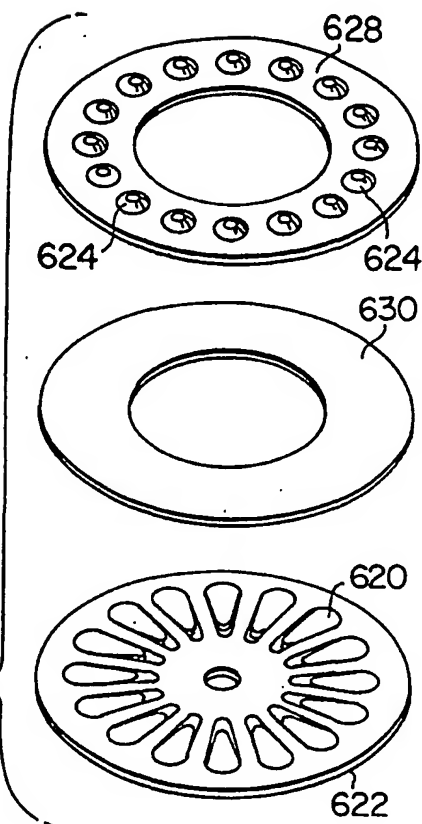


FIG. 57

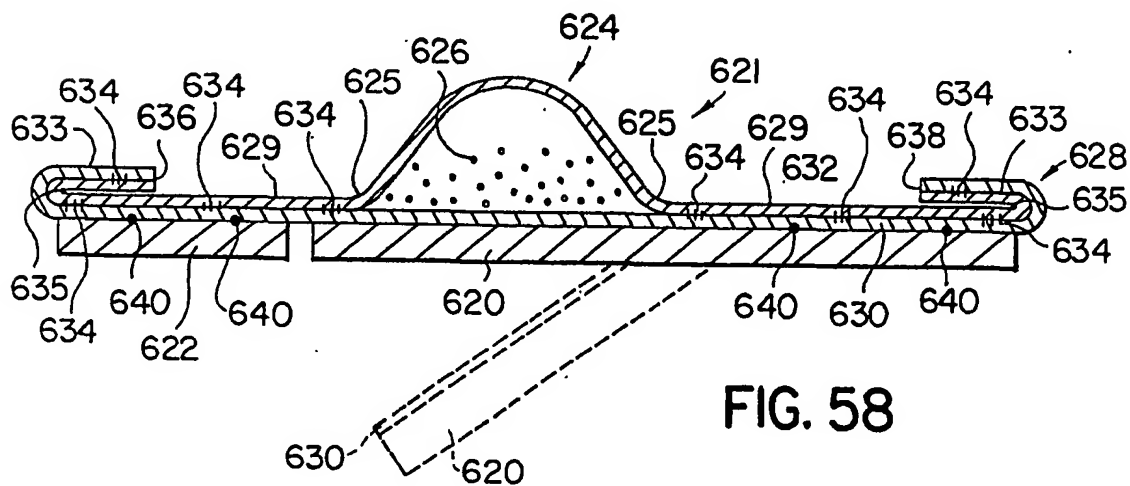


FIG. 58

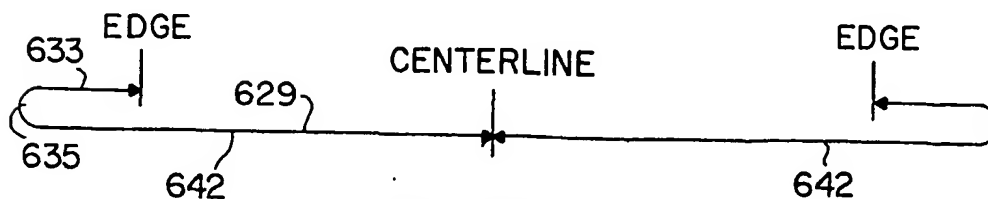


FIG. 59

FIG. 60 18/21

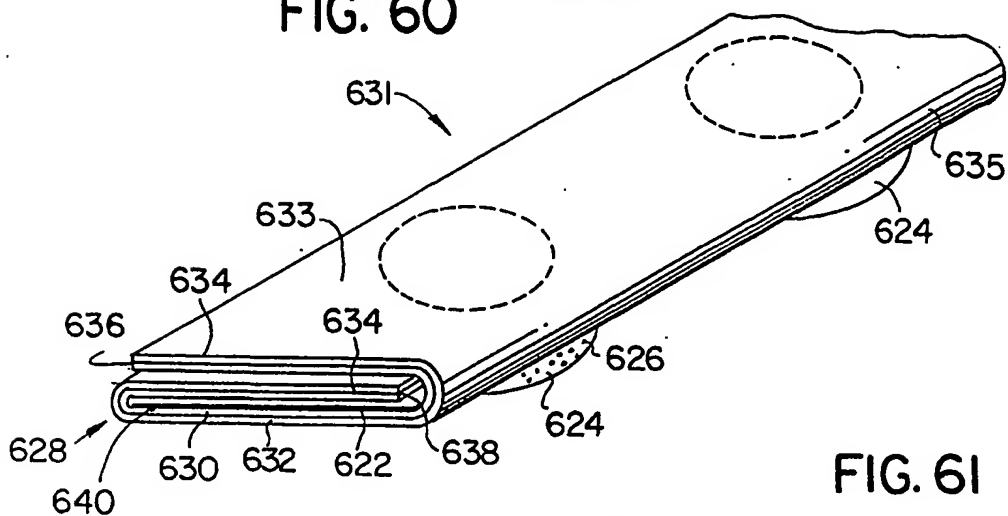


FIG. 61

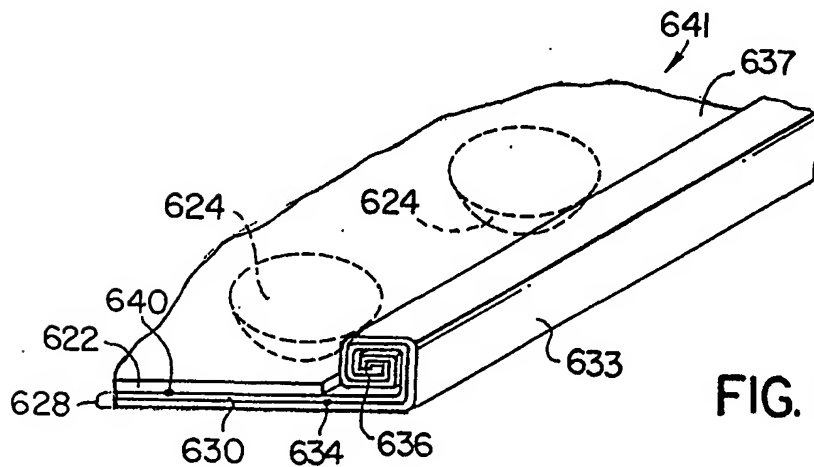
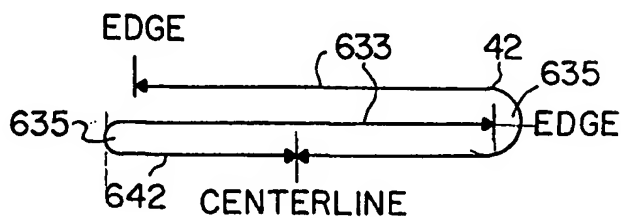


FIG. 62

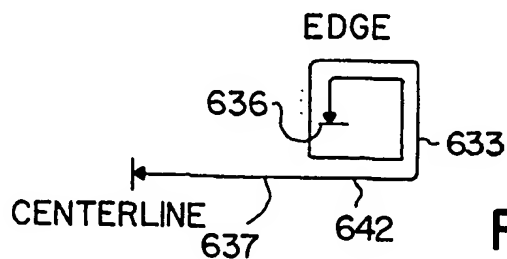


FIG. 63

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FIG. 64

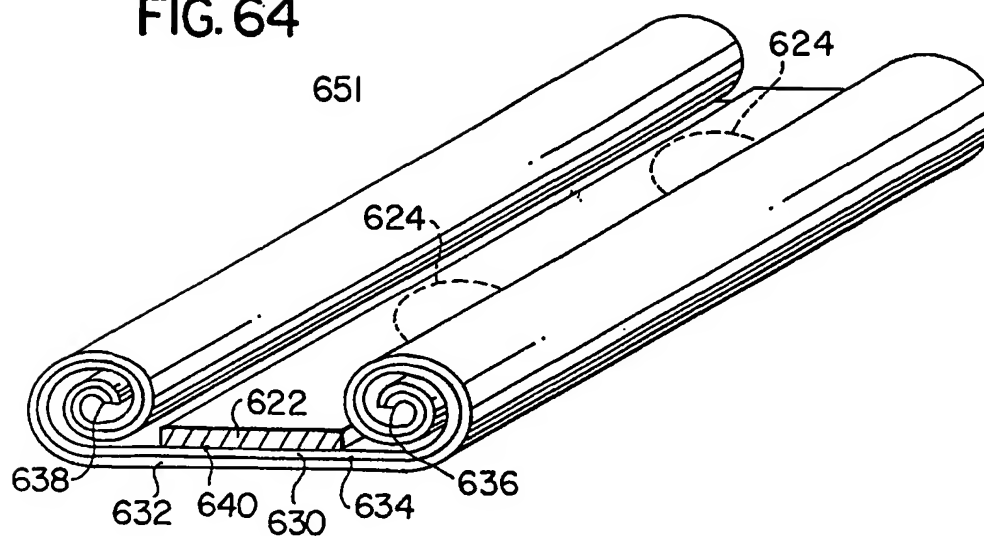


FIG. 65

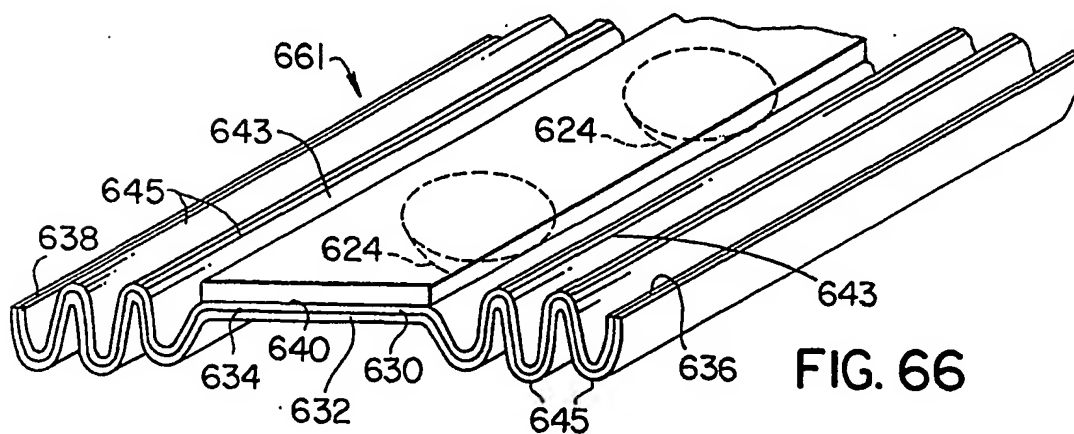
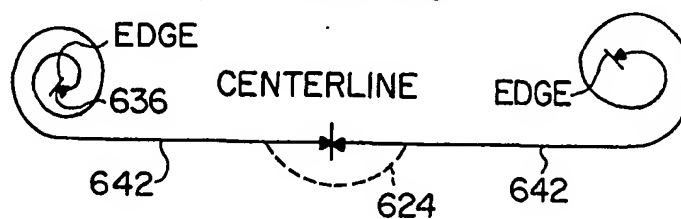


FIG. 66

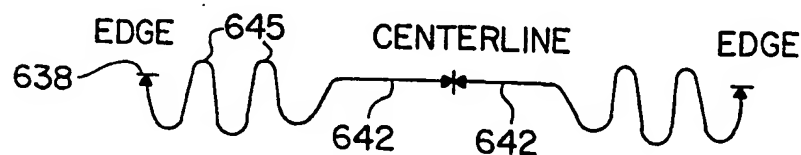


FIG. 67

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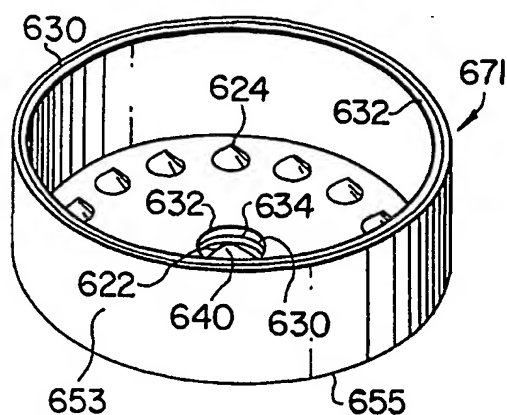


FIG. 68

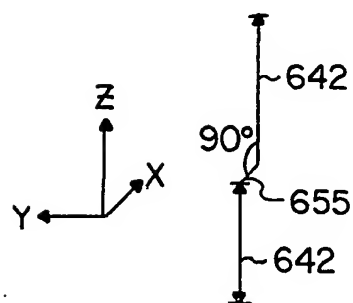


FIG. 69

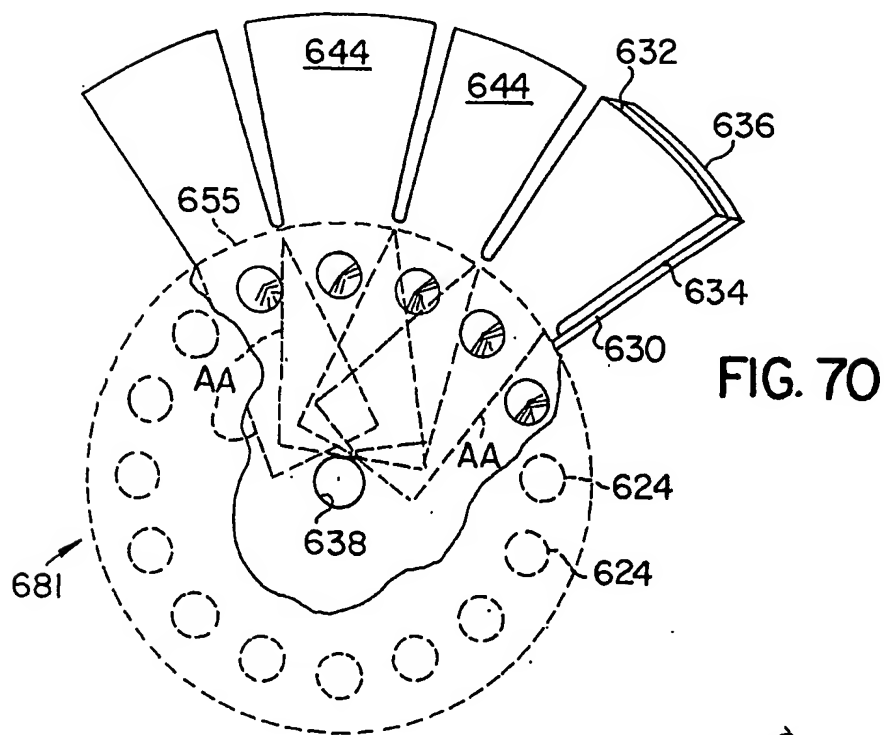


FIG. 70

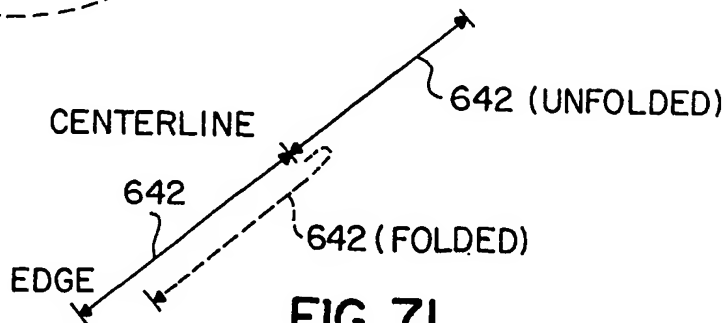
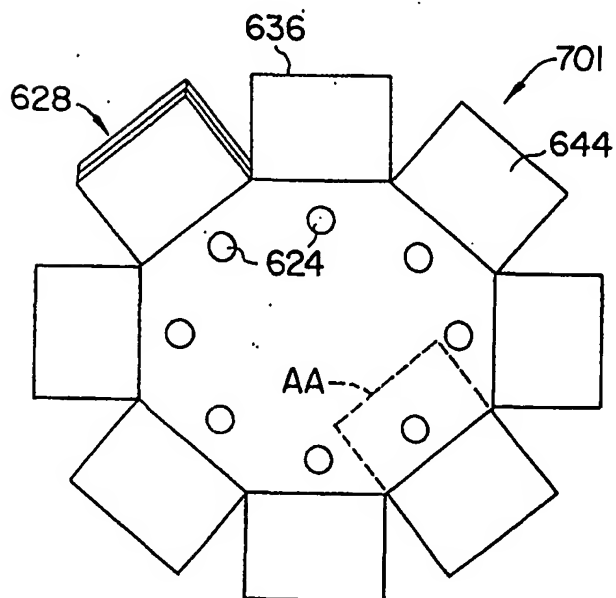
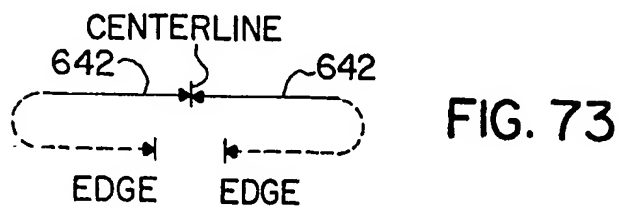
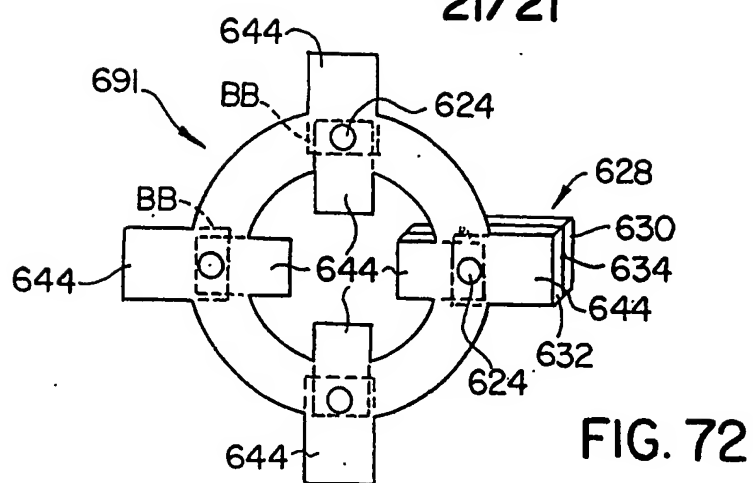


FIG. 71

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US01/08960

| A. CLASSIFICATION OF SUBJECT MATTER IPC(7) : B 65 D 83/04, 85/42 US CL : 206/539 According to International Patent Classification (IPC) or to both national classification and IPC | | |
|--|---|---|
| B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S. : 206/539, 484, 528, 531, 532, 538, 820; 128/203.12, 203.15, 203.21; 604/58 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched NONE Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WEST, blister, dose, strip, inhaler, powder, foil, medicament, pharmaceutical, pill | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | US 5727687 A (Renner) 17 March 1998, Fig 4 and supporting text. | 1-7, 31-331 |
| X | US 5778873 A (Braithwaite) 14 July 1998, Figs 16-20 and supporting text. | 8-11 |
| X | US 5924417 A (Braithwaite) 20 July 1999, Figs 16-20 and supporting text. | 8-11 |
| X, P | US 6082356 A (Stradella) 4 July 2000, Fig 1-4 & 7-8 and supporting text. | 8-11 |
| X | US 5881719 A (Gottenauer et al.) 16 March 1999, Figs 5-10 and supporting text. | 12-13 & 30 |
| X | US 5909822 A (George et al.) 8 June 1999, Figs 11-15 and supporting text. | 12-13 & 30 |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. | | |
| *A* | Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| *B* | earlier document published on or after the international filing date | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| *L* | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *O* | document referring to an oral disclosure, use, exhibition or other means | |
| *P* | document published prior to the international filing date but later than the priority date claimed | *G* document member of the same patent family |
| Date of the actual completion of the international search 22 MAY 2001 | | Date of mailing of the international search report 30 JUL 2001 |
| Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230 | | Authorized officer JOSEPH WEISS, JR. Telephone No. (703) 305-0323 |

INTERNATIONAL SEARCH REPORT

 International application No.
 PCT/US01/08960

| C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|---|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X, P | US 6116238 A (Jackson et al.) 12 September 2000, Figs 9-15 and supporting text. | 12-13 & 30 |
| X | US 5921237 A (Eisele et al.) 13 July 1999, Figs 20-22 and supporting text | 12-13 & 30 |
| X | US 5349947 A (Newhouse et al.) 27 September 1994, Figs 1-2, 4-6 and supporting text. | 14-21 |
| X | US 5622166 A (Eisele et al.) 22 April 1997, Figs 5-7& 13-16 and supporting text | 14-21 |
| X | US 3021001 A (Donofrio) 13 February 1962, Figs 1-2 and supporting text. | 1-7, 22-26, 31-33 |
| X | US 6032666 A (Davies et al.) 7 March 2000, Fig 5-7, 9-10 and supporting tex. | 27-29 |
| X | US 5823178 A (Lloyd et al.) 20 October 1998, Fig 2 and support text. | 27-29 |
| X | US 4673086 A (Braverman et al.) 16 June 1987, Fig 6 & 9 and supporting text. | 34-59 |
| X | US 1413064 A (Salfisberg) 18 April 1922, Figs 1-3 and supporting text. | 34-59 |
| A | US 5533505 A (Kallstrand et al) 9 July 1996, Peel Tab 6/25. | 1-7 & 31-33 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/08960

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US01/08960

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-7 & 31-33, drawn to A Dose Strip w/ lid closures.

Group II, claim(s) 8-11, drawn to A Dose Strip with a Unique Drum arrangement & an Inhaler for such a strip.

Group III, claim(s) 12-13 & 30, drawn to An Inhaler with a Unique Button to Blister Arrangement and a Compatible Dose Strip.

Group IV, claim(s) 14-21, drawn to A Method of Accessing a Blister Encased Dose and an Inhaler capable of Performing such method.

Group V, claim(s) 22-26, drawn to A Dose Strip with recessed layers and Cut lines/shearable layers.

Group VI, claim(s) 27-29, drawn to An Inhaler with Angular Rollers and an Advancing Mechanism.

Group VII, claim(s) 34-59, drawn to A Foil Laminate Container for Medicament doses and its Method of Making.

The inventions listed as Groups I-VII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The devices do not share specific technical feature(s) that reflects a single inventive concept/step.

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